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PB-252 309

Effects of Low Levels of Ozone and Temperature Stress

California Univ.

Prepared For
Health Effects Research Lab.

March 1976

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PB 252 309

EPA-600/1-76-001
March 1976

Environmental Health Effects Research Series

EFFECTS OF LOW LEVELS OF OZONE AND TEMPERATURE STRESS

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Health Effects Research Laboratory
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U.S. Environmental Protection Agency
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TECHNICAL REPORT DATA
(Please read Instructions on the reverse before completing)

1. REPORT NO.	2.	3. RECIPIENT'S ACCESSION NO.
EPA-600/1-76-001		

4. TITLE AND SUBTITLE
EFFECTS OF LOW LEVELS OF OZONE AND TEMPERATURE STRESS

5. REPORT DATE
March 1976 (Issuing Date)

6. PERFORMING ORGANIZATION CODE

7. AUTHOR(S)
Steven M. Horvath and Lawrence J. Folinsbee

8. PERFORMING ORGANIZATION REPORT NO.

9. PERFORMING ORGANIZATION NAME AND ADDRESS
Institute of Environmental Stress
University of California
Santa Barbara, CA 93106

10. PROGRAM ELEMENT NO.
1AA601

11. CONTRACT/GRANT NO.
EPA 68-02-1723

12. SPONSORING AGENCY NAME AND ADDRESS
Health Effects Research Laboratory
Office of Research and Development
U.S. Environmental Protection Agency
Research Triangle Park, NC 27711

13. TYPE OF REPORT AND PERIOD COVERED
7/1/1974 through 6/30/1975

14. SPONSORING AGENCY CODE
EPA-ORD

15. SUPPLEMENTARY NOTES

16. ABSTRACT

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17. KEY WORDS AND DOCUMENT ANALYSIS

a. DESCRIPTORS	b. IDENTIFIERS/OPEN ENDED TERMS	c. COSATI Field/Group
Ozone Heat Stress Cardiovascular system Respiratory System		06 F

PRICES SUBJECT TO CHANGE

18. DISTRIBUTION STATEMENT	19. SECURITY CLASS *(This Report)*	21. NO. OF PAGES
RELEASE TO PUBLIC	UNCLASSIFIED	96
	20. SECURITY CLASS *(This page)*	22. PRICE
	UNCLASSIFIED	5.00 - 2.25

EPA Form 2220-1 (9-73)

☆ U. S. GOVERNMENT PRINTING OFFICE: 1976-657-695/5390 Region No. 5-11

EPA-600/1-76-001
March 1976

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ABSTRACT

Cardiopulmonary and metabolic responses of 20 adult males (age 19-29) before, during and after a 2-hour exposure to either filtered air or 0.50 ppm ozone under four ambient conditions (25°C, 45% rh; 31°C, 85% rh; 35°C, 40% rh; 40°C, 50% rh) were determined. Exercise at 40% of the individual's $\dot{V}_{O_2\ max}$ was performed from 60-90 min of exposure. There were no cardiovascular changes due to ozone exposure but heart rate increased and stroke volume decreased with increasing heat stress. Rectal, mean body, and mean skin temperature also increased in the heat and were significantly correlated ($P < 0.05$) with WBGT. There was a decrease in vital capacity and total lung capacity due primarily to a reduction of inspiratory capacity following ozone exposure. Maximum expiratory flow (indicated by $FEV_{1.0,2.0,3.0}$, MEF50%, MEF25%, and MMEF) was also reduced following ozone exposure but, as with vital capacity, the greatest decrease occurred immediately following the exercise period in ozone. The combination of heat stress and ozone exposure resulted in significantly greater impairment of pulmonary function and more numerous reported symptoms than in the room temperature ozone exposure. The trachial-bronchial irritation caused by ozone reduces the vital capacity and maximum expiratory flow and this effect is more pronounced when the ozone exposure occurs in a hot environment.

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ACKNOWLEDGMENTS

The following were instrumental in conducting various phases of the experimental program.

Dr. John F. Bedi
Dr. Nils W. Bolduan
Dr. Barbara L. Drinkwater
Dr. Lawrence J. Folinsbee
Dr. Jeffrey A. Gliner
Dr. Bernard Gutin
Dr. Steven M. Horvath
Dr. Alan R. Morton
Dr. Pierre M. Nizet
Dr. Peter B. Raven
Dr. Jeames A. Wagner
Dr. James E. Wilkerson

Mr. James C. Delehunt
Mr. Robert S. Ebenstein
Mr. Michael B. Maron

Ms. Dorothy L. Batterton
Mr. David M. Brown
Mr. M. Fred Bush
Ms. Brigitte Hallier
Ms. Suzanne L. Hostetter
Mr. Richard R. Marcus
Mr. Douglas L. Marsh
Ms. Judy A. Matsen
Ms. Lovette Weir

We are especially appreciative of the unstinting efforts by our office staff Ms. Patricia A. Boisvert and Ms. Darlene Clement to organize our subjects and the typing of this report. To our many subjects we can only say thanks. Their cooperation made these studies possible.

SECTION I

CONCLUSIONS

Pulmonary dysfunction occurring consequent to exposure to 0.5 ppm O_3 is more pronounced following exercise and in hot ambient environments. It is necessary to perform additional studies utilizing different levels and durations of physical activities as well as other concentrations of ozone in order to determine threshold levels.

SECTION II

RECOMMENDATIONS

1. Studies similar to the present program but which incorporate a series of consecutive daily exposures to ozone should be initiated immediately.

2. Other age groups both males and females should be evaluated under conditions similar to those employed in the present study. Smokers should also be included in any sample of the population under consideration.

3. Studies should be initiated to evaluate the pulmonary effects of multiple combinations of pollutants (O_3, SO_x, NO_x etc.) at different concentration levels.

4. Since exercise of a limited magnitude induced marked pulmonary function changes, additional studies should be undertaken in which the magnitude and duration of activity would differ from the present investigation.

SECTION III

INTRODUCTION

Many pollutant episodes occur during a temperature inversion during which the ambient air pool has stagnated, therefore subjecting the human organism not only to raised levels of environmental contaminants but additionally to the stress of high ambient temperatures. Dependent upon the constituent buildup during the alert, the resultant "smog" can be generally designated: (a) reductive, consisting mainly of carbon monoxide (CO), sulfur oxides (SO_x), and particulates, usually in combination with high humidities and high or low temperatures (1-5); or (b) oxidant or photochemical, consisting mainly of carbon monoxide (CO), ozone (O_3), nitric oxides (NO_x), peroxyacetylnitrates (PAN), and particulates, usually in combination with high temperatures and low humidities (6-11).

The information available concerning CO and SO_x is generally regarded as adequate for the setting of realistic air quality standards (AQS). However, new information, by Horvath and Raven at this Institute (12-14) and Bates and Hazucha in Canada (15), regarding synergistic actions of pollutants and other variables have led to the conclusion that the simplistic view of "one pollutant, one effect" is unrealistic. In contrast to CO and SO_x, the information concerning O_3 and NO_x as single moieties is not available in a usable form for the setting of AQS. The effects of the oxidant-type smog on man's ability to work is unknown. Therefore, in this investigation we planned to study the influence of O_3 on pulmonary, cardiac, and peripheral circulatory function during rest and activity while exposed to a number of thermal heat loads.

SECTION IV

REVIEW OF LITERATURE

Early reports provided evidence for certain physiologic actions of ozone (O_3) (16-18). The primary targets of O_3 action are the lung and the respiratory tract; however, interactions with the red blood cell (RBC) and the central nervous system (CNS) have been noted (18, 19). In 1953, Belknap (in reference 65) reported pulmonary congestion consequent to exposure to high levels of ozone produced during helio-arc welding. Levels of ozone (< 1 ppm) were also found to induce respiratory tract irritation, headache, and shortness of breath (20, 21). The prominent features of the response were rapidity of onset, marked dyspnea, chest pain, and cough. Griswold et al. (22) reported that following exposure to 1.5 ppm O_3 for 30 minutes and continuation of exposure with 2.0 ppm for 90 minutes, the subject experienced dry mouth and throat, reduced ability to concentrate and think, altered taste sensation, substernal pain, and paresthesia of the extremities. The long-term sequelae were a loss of appetite, sleepless and uncomfortable nights, cough developing two days after exposure and persisting for two weeks, and expectoration of clear mucus. At the end of the acute exposure subjects had an initial 17% reduction in 3-second vital capacity (VC) which was still 7% below control levels 22 hours later. The maximum breathing capacity was only 3% reduced.

Federal threshold limit values (TLV) and air quality standards (AQS) have been based upon pulmonary data (23) and some industrial observations (24). When 12 subjects were exposed to 0.6 to 0.8 ppm O_3 for 2 hours, a significant reduction in pulmonary diffusing capacity to CO ($D_{L_{CO}}$) occurred with only slight changes in VC and forced expiratory volume (FEV), although diminution of $FEV_{0.75} \times 40$ estimated maximal voluntary ventilation (MVV) and throat irritation occurred (25). These findings suggested that O_3 exerted its initial influence at the level of the alveolar membrane. The changes were transient, persisting for less than 24 hours after the subjects returned to clear air environments. Challen et al. (66) reported the presence of upper respiratory symptoms in 11 of 14 welders exposed daily to O_3 levels of 0.8 to 1.7 ppm.

The symptoms disappeared following reduction of the levels to 0.2 ppm. It was primarily from this data that the industrial TLV of 0.1 ppm over 8 hours was obtained. Stokinger (26) reported that exposures to 0.13 ppm maximum daily value of total oxidant caused an increased number of asthmatic attacks in 5% of asthmatic subjects. By comparison, exposures of nonasthmatic human volunteers to 0.3 ppm O_3 for 8 hours resulted in nose and throat irritation and to 0.5 ppm for 3 hours each day gave decreased $FEV_{1.0}$ after 8 weeks, but 0.2 ppm was without effect after 12 weeks of 3-hour daily exposures. These were data that served as the criteria for AQS for O_3 of 0.08 ppm for a 1-hour maximum (26).

Results of other experimental exposures of man (7, 23, 24, 27) to low levels of ozone confirmed the findings outlined above. A significant increase in airway resistance (R_{aw}) was observed when resting subjects were exposed to 1.0 ppm for 1 hour (23, 24). However, few investigations (27, 41, 42, 43) have considered the combined effect of ozone and exercise. Bates et al. (27) studied the effects of 0.75 ppm O_3 on 10 normal subjects during rest for 2 hours and on only 3 subjects during 15 minutes of light exercise followed by a rest for 15 minutes during a similar 2-hour exposure. The resting subjects reported substernal soreness and cough, while a few had symptoms of pharyngitis and dyspnea. Objectively, it was observed that the subjects had a significant fall in maximum static elastic recoil pressure of the lung, a significant increase in pulmonary resistance with a decrease in flow rates measured at 50% vital capacity. However, unlike a previous study (25) no significant reduction in CO uptake was found. The investigators concluded that large and small airway effects can be observed before changes in diffusion capacity ($D_{L_{CO}}$) become apparent. This conclusion was somewhat different from that obtained in the previous study (25). The three subjects that exercised reported symptoms far earlier during the exposure and all pulmonary effects were more marked. Other studies have indicated that the effects of ozone are not entirely restricted to the respiratory tract; however, the mechanisms by which these extrapulmonary effects occur are unknown.

The results of the above reported experiments suggested that exposures to O_3 above 0.75 ppm for 2 hours or more caused physiological impairment even if the subjects are resting quietly. The combination of an exercise intensity sufficient to elevate ventilatory volumes to 20 liters/min significantly decreased the time of exposure at which these effects were observed and suggested that the levels of ozone now being found within urban environments (30, 31) might induce significant physiologic impairment. It has also been reported that during exposures to 1 ppm O_3 for 10 minutes the rate of oxyhemoglobin desaturation was reduced (28), while Lagerwerff (29) reported that visual acuity was significantly impaired at ozone levels from 0.2 to 0.5 ppm.

Following 30 minutes of exposure to 15 ppm O_3, rabbits showed a 50% reduction in oxygen uptake, which remained below normal for 2 days. Repeated exposures resulted in similar responses, but, most interesting, recovery was more rapid following each successive exposure. Ozone at 2 ppm for 3 hours produced similar responses in rats (32). The rabbits were able to compensate to 1-hour exposures daily for 4 months; however, with continued exposure a gradual deterioration in pulmonary performance was found.

Other factors affect the inherent toxicity of O_3. Young mice were found to be more susceptible to the acute toxic effects of O_3 than older animals (33), while a 15°F rise in ambient temperature resulted in an increased susceptibility to O_3 in both mice and rats. When rats rested in 1 ppm O_3, no acute effects were observed; however, the concentration became lethal when the rats were exercised for a few minutes each hour during exposure (18). Mice infected with *Klebsiella pneumoniae* and then exposed to O_3 showed shortened survival time and increased mortality (34), and prior O_3 exposure decreased the resistance to respiratory infection. More recent animal experiments have been aimed primarily at the mechanism of action of O_3 (35, 36, 37, 38) rather than determination of critical levels. However, Yokoyama and Frank (39) have evaluated the findings of Vaughan et al. (40), who observed

that in muzzled dogs 100% of inhaled ozone was extracted by the upper respiratory tract, indicating that 0_3 was not present in the alveoli. Yokoyama and Frank demonstrated that, although nose breathing resulted in removal of 0_3 from airstream more efficiently than the mouth at low flow rates, when high flow rates and mouth breathing were utilized the alveoli were exposed to significant amounts of ozone even though the rate of "uptake" of 0_3 is reduced as the rate of flow increases. These findings emphasized the need to determine the response of the lung to low levels of ozone at raised levels of ventilatory exchange as well as during periods of elevated ambient conditions.

SECTION V

GENERAL OBJECTIVES AND SPECIFIC AIMS

This study was designed to determine the effects of 0.3 to 0.5 ppm ozone (O_3) on the metabolic, thermoregulatory and cardiopulmonary systems of young men (18-30 years of age) while they were exposed to different ambient temperature conditions. These conditions ranged from normally cool (25°C and 45% rh) through warm wet (31°C and 85% rh) to hot dry (40°C and 50% rh). By including exercise levels of approximately 40-45% of each subjects maximal capability it was anticipated that it would be possible to evaluate the effect of these conditions on man when he was at rest or at work. The findings obtained from this investigation would enable regulatory agencies to evaluate a level of 0.5 ppm O_3 as a possible national level guideline to be used for the health protection of the general population.

SECTION VI

RESEARCH METHODS

SUBJECTS

Twenty-one young healthy males (ages 18-30 years) were selected as subjects from some thirty volunteers. All volunteers were nonsmokers [confirmed by blood carboxyhemoglobin (HbCO) analysis] and were drawn from the student population of the University of California, Santa Barbara campus. Subjects were completely informed as to the purpose of the tests and signed University consent forms to act as human subjects. Each volunteer was medically screened. A medical history questionnaire, a resting 12-lead electrocardiogram, an exercise electrocardiogram (V_4) up to 160 beats each minute, determination of basal metabolic rate (BMR), and a battery of clinical spirometric tests were used in evaluating each subject. Following the screening the subjects performed a maximal aerobic capacity ($\dot{V}_{O_2\ max}$) test on a treadmill. Table 1 summarizes pertinent physical and physiological data of the participating subject. Following the maximal performance test each subject was trained (two 1-hour sessions on separate days) in the procedures being utilized for the determination of cardiovascular, pulmonary and peripheral circulatory functions.

EXPERIMENTAL DESIGN

The following basic approach was used with all exposure conditions being subject to random order presentation. Two groups of subjects (designated A and B) were exposed to eight separate conditions. Exposure to each condition was separated by a minimum of one week for each individual subject. The exposure conditions for both the pollutant and ambient environments are outlined in Table 2.

Table 1. SUBJECT INFORMATION

Subj No.	Age, yr	Ht, cm	Wt, kg	BSA, m^2	VC, liters	$FEV_{1.0}$, liters	$FEV_{3.0}$, liters	IC, liters	ERV, liters	RV/TLC, %	MVV, liters /min	$\dot{V}_{O2}$ max, liters /min
7495	19	190.25	91.6	2.20	8.45	6.99	8.34	6.13	2.32	20	202	4.22
7493	22	187.6	81.2	2.02	6.60	5.30	6.45	4.02	2.58	15	169	3.28
7496	24	178.6	74.8	1.92	6.09	4.76	6.02	4.44	1.65	24	219	3.01
7510	20	177.5	64.3	1.78	5.12	4.77	5.01	3.34	1.17	26	164	3.59
7505	21	178.1	84.0	2.02	5.72	4.23	5.55	3.59	2.14	22	193	4.35
7519[a]	22	175.5	65.4	1.80	5.94	4.66	5.83	3.35	2.60	32	136	—
7522	21	176.5	70.2	1.87	5.25	4.37	5.23	3.32	1.93	23	157	3.95
7504	21	180.6	75.8	1.96	5.40	4.38	5.40	3.29	2.11	20	162	3.55
7555[a]	21	161.8	58.0	1.61	4.28	3.72	4.18	2.51	1.77	22	173	—
7516[a]	19	175.5	55.7	1.69	5.75	4.87	5.75	4.44	1.31	32	144	2.30
7561	21	180.3	81.0	2.02	5.61	4.21	5.27	4.08	1.53	23	182	4.04
7659	21	182.0	77.0	1.98	7.36	4.37	6.91	4.66	2.70	23	148	3.97
7613[a]	22	161.8	55.6	1.59	4.47	3.84	4.46	3.02	1.45	32	179	2.50
7650	20	184.9	81.0	2.05	6.42	5.31	6.31	4.47	1.95	26	198	4.21
7658[a]	20	182.1	91.0	2.13	6.24	5.12	6.07	4.65	1.59	23	202	4.38
7674	20	173.2	77.6	1.93	6.36	4.93	6.15	4.23	2.12	25	137	4.09
7684	20	190.5	83.4	2.10	6.22	4.75	6.21	3.60	2.62	31	191	4.37
7822	23	179.3	69.6	1.88	5.77	4.23	5.60	3.62	2.09	30	205	3.57
7823	23	165.1	53.0	1.57	4.31	3.96	4.26	2.97	1.33	31	214	2.7
7887	20	172.1	64.8	1.82	5.20	4.49	5.10	2.99	2.07	26	155	3.36
7829	20	179.6	64.2	1.82	4.34	4.16	4.34	2.67	1.66	23	198	4.12

[a] Subjects not completing the test series.

Table 2. EXPOSURE CONDITIONS[a]

Exposure[b]	Temperature and relative humidity[c]			
	Set			
	B1	B2	B3	B4
Ambient air (Control exposures)	25°(45) (Code 1)	31°(85) (Code 2)	35°(40) (Code 3)	40°(50) (Code 4)
Ozone (0.44 - 0.57 ppm) (Experimental exposures)	25°(45) (Code 5)	31°(85) (Code 6)	35°(40) (Code 7)	40°(50) (Code 8)

[a] The equivalent WBGT temperatures for 1, 2, 3, and 4 conditions are respectively 64.4, 85.2, 80.0 and 92.0°F and are respectively similar for 5, 6, 7, and 8.

[b] Exposure was for a 2-hour period.

[c] All temperatures are Celsius. Percentage relative humidity listed in parentheses (%).

EXPERIMENTAL PROTOCOL

Groups A and B underwent the routines outlined in Table 3.

Table 3. EXPERIMENTAL ROUTINE

	Control Period	Exposure Periods[a]								Recovery Period
Code Number		1	2	3	4	5	6	7	8	
Group A	Pre-Exp. Tests	R	R	R	R	W	W	R	R	Post-Exp. Tests
Group B	Pre-Exp. Tests	R	R	W	W	R	R	R	R	Post-Exp. Tests

[a] Each section = 15 minutes duration, R = sitting rest; W = work at 45% $\dot{V}O_{2\ max}$.

Pre- and post-exposure tests lasted approximately 1-hour each. During exposure, the group A subjects rested in the sitting position for 1-hour then exercised for 30 minutes on a motor-driven treadmill at approximately 45% $\dot{V}O_{2\ max}$ followed by a 30-minute seated rest. Group B underwent a similar 2-hour exposure except that the exercise sessions occurred in the second half-hour of exposure (Table 3).

Each subject was scheduled for eight experimental sessions. Exposures occurred throughout the day although each individual was always scheduled at the same time of day. On arrival at the Institute, the subject was weighed nude and then connected to the appropriate

monitoring leads for temperatures and electrocardiogram. Clothing worn during the experiments consisted of tennis shoes, socks, shorts, and supporter. Each subject was given a clinical chest examination and seated for withdrawal of a 12-ml pre-exposure venous blood sample. The subject then performed a battery of pulmonary tests on a 13.5-liter chain-compensated spirometer (W. E. Collins) and in a volume body plethysmograph (W. E. Collins). The subject then entered the exposure chamber, set at the required ambient conditions, and was connected to appropriate monitoring cables. The 2-hour exposure was divided for convenience into eight 15-minute segments (numbered 1-8) (Table 3). Each period for either group A or B was utilized as outlined in the following summary:

SUMMARY OF PROTOCOL UTILIZED DURING EXPOSURES

PERIOD 1

GROUP A & B Minutes 0-2 -- Forearm blood flow.

Minutes 2-4 -- Ventilatory volume ($\dot{V}_E$), O_2 and CO_2 percentages, heart rate (HR), tidal volume (V_T), and respiratory frequency (f_R). Temperatures: room (T_{rm}), radiant (T_r), mean skin ($\overline{T}_{sk}$), and rectal (T_{re}).

Minutes 4-6 -- Cardiac output ($\dot{Q}$), blood pressure (BP), and HR.

Minutes 6-10 -- Steady-state diffusion capacity to carbon monoxide ($D_{L_{CO}}$).

Minutes 10-15 -- Pulmonary function tests: forced vital capacity (FVC); forced expired volume at 1.0, 2.0, and 3.0 seconds ($FEV_{1.0,2.0,3.0}$); flow at 50% and 25% vital capacity (MEF50%, MEF25%); expiratory reserve volume (ERV); and inspired capacity (IC). Closing volume with slow vital capacity (VC) in duplicate. T_{rm}, T_r, $\overline{T}_{sk}$, and T_{re}.

PERIOD 2

Group A & B Sitting rest

Minutes 5-6 -- HR, BP, $\overline{T}_{sk}$, T_{re}, T_{rm}, T_r and forearm blood flow.

Minutes 10-11 -- HR, BP, $\overline{T}_{sk}$, T_{re}, T_{rm}, and T_r.

Minutes 11-14 -- FVC, $FEV_{1.0,2.0,3.0}$, ERV, IC, MEF50%, and MEF25%. Closing volume with slow VC in duplicate.

PERIOD 3

Group A Sitting rest -- BP, HR, $\overline{T}_{sk}$, T_{re}, T_{rm}, and T_r (each at 5, 10, and 15 min).

Exercise -- BP, HR, $\overline{T}_{sk}$, T_{re}, T_{rm}, and T_r (each at 5, 10, and 15 min).

PERIOD 4

Group A Sitting rest

Minutes 0-2 -- Forearm blood flow.

Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, HR, V_T, f_R, T_{rm}, T_r, $\overline{T}_{sk}$, and T_{re}.

Minutes 4-6 -- $\dot{Q}$, BP, and HR.

Minutes 6-10 -- Steady state $D_{L_{CO}}$.

Minutes 10-15 -- FVC, $FEV_{1.0,2.0,3.0}$, MEF50%, MEF25%, ERV, and IC. Closing volume with slow VC in duplicate. T_{rm}, T_r, $\overline{T}_{sk}$, T_{re}, and HR.

Group B Exercise

Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, T_{rm}, T_r, $\overline{T}_{sk}$, T_{re}, and HR.

Minutes 4-6 -- $\dot{Q}$, BP, and HR.

Minutes 6-10 -- Steady-state $D_{L_{CO}}$.

Minutes 10-15 -- T_{rm}, T_{rad}, $\overline{T}_{sk}$, T_{re}, and HR.

PERIOD 5

Group A Exercise -- BP, HR, $\overline{T}_{sk}$, T_{re}, T_{rm}, and T_r (each at 5, 10, and 15 min).

Group B Sitting -- BP, HR, $\overline{T}_{sk}$, T_{re}, T_{rm}, and T_r (each at 10 and 15 min). Forearm blood flow at 10 min.

PERIOD 5 (Continued)

Minutes 3-10 -- FVC, $FEV_{1.0,2.0,3.0}$, MEF50%, MEF25%, ERV, and IC. Closing volume with slow VC in duplicate.

PERIOD 6

Group A Exercise

Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, T_{rm}, T_r, $\overline{T}_{sk}$, T_{re}, and HR.

Minutes 4-6 -- $\dot{Q}$, BP, and HR.

Minutes 6-10 -- Steady-state $D_{L_{CO}}$.

Minutes 10-15 -- T_{rm}, T_r, $\overline{T}_{sk}$, T_{re}, and HR.

Group B Sitting rest

Minutes 0-2 -- Forearm blood flow

Minutes 2-4 -- $\dot{V}_E$, O_2, and CO_2 percentages, V_T, f_R, HR, T_{rm}, T_r, $\overline{T}_{sk}$, and T_{re}.

Minutes 4-6 -- $\dot{Q}$ and BP.

Minutes 6-10 -- Steady-state $D_{L_{CO}}$.

Minutes 10-15 -- FVC, $FEV_{1.0,2.0,3.0}$, MEF50%, MEF25%, ERV, and IC. Closing volume with slow VC in duplicate. T_{rm}, T_r, $\overline{T}_{sk}$, T_{re}, and HR.

PERIOD 7

Group A Sitting rest -- BP, HR, $\overline{T}_{sk}$, T_{re}, T_{rm}, and T_r (each at 10 and 15 min). Forearm blood flow @ 10 min.

Minutes 3-10 -- FVC, $FEV_{1.0,2.0,3.0}$, MEF50%, MEF25%, ERV, and IC. Closing volume with slow VC in duplicate.

Group B Sitting rest -- BP, HR, $\overline{T}_{sk}$, T_{re}, T_{rm}, and T_r (each at 5, 10, and 15 min). Forearm blood flow @ 5 min.

PERIOD 8

Group A & B Sitting rest

Minutes 0-2 -- Forearm blood flow.

Minutes 2-4 -- $\dot{V}_E$, O_2 and CO_2 percentages, V_T, f_R, HR, T_{rm}, T_{re}, $\overline{T}_{sk}$, and T_r.

PERIOD 8 (Continued)

Minutes 4-6 -- $\dot{Q}$, BP, and HR.

Minutes 6-10 -- Steady-state $D_{L_{CO}}$.

Minutes 10-15 -- FVC, $FEV_{1.0,2.0,3.0}$, MEF50%, MEF25%, ERV, and IC. Closing volume with slow VC in duplicate. HR, BP, T_r, $\overline{T}_{sk}$, T_{re}, and T_{rm}.

At the end of the 2-hour exposure, the subject was allowed into the FA atmosphere of the laboratory, disconnected from the monitoring wires and seated on a chair. The attending physician immediately gave a clinical chest examination, and 4 minutes after exposure another 12-ml venous blood sample was obtained. The subject then repeated the battery of spirometric tests. Following these post-exposure tests, the subject completed a 33-item questionnaire, was weighed nude, and then allowed to leave the laboratory on permission of the examining physician.

MEASUREMENT TECHNIQUES

Metabolic measurements were made using open-circuit indirect calorimetric techniques (44). Ventilatory volumes were monitored by collecting timed volumes in a 120-liter chain-compensated spirometer. Aliquot gas samples were analyzed for O_2% and CO_2% in a Quintron gas chromatograph calibrated against standard Haldane analyzed gases. Accuracy of analysis was ±0.02% for CO_2 and ±0.05% for O_2. Incorporation of appropriate temperature and barometric pressure corrections with the raw metabolic data in the Institutes batch process computer analysis resulted in the determination of all other metabolic parameters (see Glossary).

Copper-constantan thermocouples were used to monitor rectal temperature (T_{re}) at the depth of 12 cm into the rectum. Mean skin temperature ($\bar{T}_{sk}$) was obtained from a weighted average of seven skin surface temperatures (forehead, arm, finger, thigh, calf, chest and abdomen). In addition, globe temperature and chamber air temperature as well as a continuous monitor of relative humidity provided a description of environmental conditions in terms of WBGT. The thermocouple temperatures were recorded by a Honeywell multichannel digital recorder and simultaneously recorded by a laboratory computer (PDP-12). Temperature parameters were used in the calculation of thermoregulatory changes as outlined in the Glossary section (45). All temperatures were measured with an accuracy of ±0.1°C.

Cardiac output was determined using the carbon dioxide rebreathing technique of Defares (46) as modified by Jenous et al. (47). Calculation of mixed venous CO_2 (PV_{CO_2}) was performed by the extrapolation method (48) utilizing the laboratory computer display. This enabled the operator to discard those points which obviously were not fitted to the general rebreathing pattern and thereby obtain a better estimate of the point of equilibrium. The coefficient of variation for repeated measurements on one subject within a period of one hour was 10%. Tidal volume and respiration rate were determined during the measurement of end tidal carbon dioxide. Blood pressure was obtained by the indirect Riva Rocci

method and heart rate from V_4 lead recorded on a Sanborn 500 Viso-Cardiette electrocardiograph. All electrocardiogram tracings were read by the Institute's cardiologist. An oscilloscope display of the electrocardiogram was continuously monitored. Estimation of forearm blood flow was made using the strain-gauge plethysmographic techniques of Whitney (49). The $D_{L_{CO}}$ was determined using the steady-state technique of Filley et al. (50) as modified by Bates et al. (51). The coefficient of variation of $D_{L_{CO}}$ determination for repeat measurements on one subject at rest was 12% and at moderate exercise (40% $\dot{V}O_{2\ max}$) was 6%. Combinations of the cardiovascular and metabolic data enabled the calculations of various cardiorespiratory parameters, i.e. diffusion/perfusion ratio and ventilation/perfusion ratio (see Appendix A for a sample printout of measured and calculated data).

The procedures outlined by Kory et al. (52) were used for pulmonary function tests. A 13.5-liter chain-compensated spirometer (W. E. Collins Co.) was used for pre- and post-exposure pulmonary measures and a Wedge spirometer (Med Science Electric Co.) connected via appropriate pre amplifiers to a multichannel pen recorder was used during the exposure period for the determination of FVC, $FEV_{1.0,2.0,3.0}$, IC, ERV, MEF50%, MEF25% and mid portion of the FVC (MMEF). The helium dilution technique was used for the measurement of residual volume (RV) before and after exposure and total lung capacity (TLC) was calculated using this value. MVV was determined prior to and following exposure. All volumes and flow rates measured in these tests were corrected to BTPS. During exposure duplicate determinations of closing volume (CV) and slow vital capacity (SVC) using a helium bolus technique (53, 54) were made. Calculation of other pulmonary function parameters were performed by computer (see Appendix B). Comparison of volumes measured on numerous subjects at the same time of day on the chain-compensated spirometer and the Wedge spirometer indicated that at volumes between 3 and 6 liters the wedge spirometer was consistently higher by 200 ml — a difference ranging from 3-7%. However, as comparisons between values obtained by the two methods were not made, corrected values were not utilized. The coefficients of variation of repeat measurements of vital capacity

on one subject made at hourly intervals during one day ranged from 0.9% to 5.0%, whereas the coefficient of variation of repeated measurements of closing volume would range from 10% to 30%, which is consistent with recently reported results (55, 56).

CHAMBER DESIGN AND CONTROL

A 1.8 m wide by 2.4 m long by 2.6 m high double-walled flow-through acrylic environmental chamber was utilized for chamber exposures. Inlet air was filtered through activated charcoal, Baralyme, soda lime, Drierite, and gauze before entering the chamber. Air was forced into the chamber at flow rates ranging from 200 liters/min to 500 liters/min resulting in exchange turnover in the chamber ranging from once every 56 min to once every 22 min. Minimal air movement across the subject occurred due to the dispersive design of the inflow air. Automatic regulated heating dehumidifier and air conditioner allowed for appropriate temperature control. When needed for humidification steam was piped directly into the air inflow. However ozone was put directly into the chamber and mixed with the chamber air by blow fans. The chamber was equipped with a small motor-driven treadmill, chair and appropriate equipment for the subject to perform the tests without experimenter assistance. All rubber components were protected from ozone attack by a weekly coating of anti-oxidant (Armor-all).

Ozone was generated (Ozone Research Inc.) outside the chamber utilizing pure oxygen to remove the possibility of nitrogen oxide production. Ozone concentration was continuously monitored utilizing the chemiluminescence technique. The monitor (McMillan Corp.) was calibrated prior to each ozone exposure using a standard calibrated ozone generator (Monitor Labs Inc.). In addition, an aliquot sample was drawn through midget impingers once each exposure for the determination of ozone concentration by the neutral buffered potasium iodide method (57). The mean 2-hour exposure ozone concentration measured by the chemiluminescence technique was 0.507 ± 0.04 and that obtained utilizing aliquot samples and chemically analyzed was 0.498 ± 0.07 ppm. The ozone sampling inlet was placed near to an average position of

the subject's head during exposure (always withing 24 inches). Exposure incorporating combinations of high temperatures and humidities resulted in a rapid breakdown of ambient ozone. In order to maintain the ozone levels during the cyclic operation of the dehumidifiers and air conditioners a second ozone generator was built by Institute personel using the design outlined by Hazucha (58). This backup generator consisted of two 12,000-volt transformers connected in series discharging through pure oxygen. The ozone output of this generator was in excess of 100 ppm.

STATISTICAL EVALUATION OF DATA

Data were analyzed by a series of analyses of variance. For pre- and post-test measurements, a three-factor factorial analysis of variance with repeated measures across time, environment and ambient air was used; for the pre-exercise and post-exercise periods, a two-factor analysis of variance with repeated measures across environment and ambient air. In all cases where a significant interaction was observed, a test was made of the simple main effects followed by a Newman-Keuls test of ordered means where appropriate. Prior to the collection of data, it was decided to make an a priori comparison of responses at codes 4 and 8 regardless of the outcome of the *F* test(59), since code 8 was the most extreme condition in O_3 and code 4 was the FA equivalent. All hypotheses were tested for significance at an alpha level of 0.05.

SECTION VII

RESULTS AND DISCUSSION

RESULTS

The mean values of pulmonary function measurements made before and after exposure under four environmental conditions to filtered air (codes 1-4) as well as to 0.50 ppm ozone (codes 5-8) are summarized in Table 4 and Figs. 1a through 1e. VC declined an average of 350 ml following ozone exposure ($P < 0.05$) regardless of the environment when compared with the measurement made before exposure. There was no change in VC following exposure to filtered air in any environment except in condition B4 (see Table 2), where the VC declined whether ozone was breathed or not. However, the decrease in VC in condition B4 was less with FA than in comparable exposure with O_3. The decline in vital capacity was primarily due to a decline in inspiratory capacity. IC was reduced an average of 300 ml ($P < 0.01$) following ozone exposure but did not change following filtered air. There were no significant changes in ERV in any condition. The resting expiratory position of the lungs (FRC) tended to increase following the exposure regardless of the conditions. The change was small (average 109 ml) and the physiological significance is questionable as neither ERV or RV, whose sum comprises the FRC, showed significant changes. The total lung capacity was reduced an average of 250 ml ($P < 0.05$) primarily due to the decrease in inspiratory capacity. However, the ratio RV/TLC increased regardless of the exposure conditions.

The flow-related pulmonary function measurements all showed significant decreases following the ozone exposure regardless of the thermal conditions. The forced expired volume was reduced following ozone exposure whether measured at 1, 2, or 3 sec. The greatest reduction (500 ml) ($P < 0.01$) occurred at 1 sec ($FEV_{1.0}$). The decrease in $FEV_{2.0}$ (450 ml) and $FEV_{3.0}$ (350 ml) was smaller. The average decline in $FEV_{3.0}$ is of the same magnitude as the decrease in FVC (350 ml) and can probably be accounted for on this

Table 4. PULMONARY CHANGES PRIOR TO AND AFTER EXPOSURE (2 HOURS) TO FILTERED AIR OR 0.5 ppm OZONE AT VARIOUS ENVIRONMENTAL CONDITIONS[a,b]

	Filtered Air							
	Code 1		Code 2		Code 3		Code 4	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
VC, ml	6081±410	6096±415	6096±356	6106±426	6181±386	6121±404	6091±405	5943±371
$FEV_{1.0}$, ml	4782±165	4714±329	5115±290	5029±322	5020±406	4863±376	5043±248	4920±152
$FEV_{2.0}$, ml	5714±338	5761±308	5907±385	5878±426	5814±397	5659±390	5890±416	5721±253
$FEV_{3.0}$, ml	6016±433	6053±393	6086±391	6100±470	6034±393	5969±409	6096±434	5971±333
IC, ml	3843±303	3824±265	3855±214	3848±230	3898±231	3750±191	3812±221	3744±243
ERV, ml	2238±190	2272±223	2241±179	2300±215	2283±243	2370±246	2273±219	2199±168
FRC, ml	3951±229	4080±180	3993±160	4081±134	3969±328	4165±276	4092±224	4293±238
RV, ml	1713±159	1808±146	1752±103	1781±134	1687±188	1795±138	1820±139	2094±144
TLC, ml	7794±502	7904±405	7849±337	7888±350	7867±509	7916±433	7911±429	8037±433
RV/TLC, %	22.0±1.6	23.2±2.2	22.6±1.6	23.0±2.3	21.3±1.6	22.9±1.8	23.2±1.8	26.2±1.6
MMEF, liters/sec	5.09±0.29	4.80±0.40	5.35±0.43	5.28±0.34	5.12±0.69	4.94±0.52	5.28±0.44	5.44±0.39
MEF50%, liters/sec	5.11±0.54	5.37±0.55	5.51±0.43	5.10±0.46	5.76±0.67	5.24±0.54	5.92±0.45	5.66±0.55
MEF25%, liters/sec	2.59±0.32	2.39±0.33	2.62±0.26	2.37±0.27	2.68±0.47	2.33±0.27	2.88±0.44	2.51±0.35
R_{aw}, cm H_2O/liters·sec	1.68±0.20	1.82±0.17	1.76±0.20	1.94±0.24	1.73±0.17	1.85±0.19	1.86±0.25	1.83±0.08
MVV, liters/min	219±13	208±15	222±9	219±9	219±12	212±11	226±10	210±7

[a] Subjects walked at approximately 40% $\dot{V}_{O_2\ max}$ from 60-90 minutes of exposure.

[b] $P<0.05$ for underlined data: see Notes in right column and STATISTICAL EVALUATION OF DATA subsection.

(Continued on page 22)

Table 4. (Continued)

0.5 ppm Ozone								Notes
Code 5		Code 6		Code 7		Code 8		
Pre	Post	Pre	Post	Pre	Post	Pre	Post	
6123±395	5938±407	6100±372	5892±398	6173±395	5754±394	6099±395	5509±276	4 > 8
5052±329	4649±282	4903±281	4570±196	4870±247	4313±209	4997±341	4284±202	FA > O_3
5794±386	5508±380	5712±374	5422±339	5684±374	5178±280	5791±395	5093±226	FA > O_3
5984±387	5772±409	5953±374	5750±381	5940±390	5549±349	5976±398	5348±252	FA > O_3
3907±217	3677±204	3877±197	3790±255	3898±283	3552±319	3950±254	3434±181	FA > O_3
2217±264	2265±283	2228±190	2103±229	2276±214	2200±146	2150±210	2082±183	No change
4193±353	4148±278	4103±250	4218±360	4152±223	4150±209	4027±274	4167±286	Pre < Post
1976±186	1883±193	1876±126	2115±311	1877±189	1950±176	1878±192	2084±314	No change
8099±526	7821±455	7976±438	8008±606	8050±433	7704±516	7977±488	7593±439	FA > O_3
24.3±1.5	24.2±2.1	23.5±1.3	26.0±2.5	23.4±2.1	25.3±1.5	23.5±2.0	27.0±2.9	Pre < Post
5.29±0.56	4.57±0.44	5.06±0.39	4.52±0.32	4.86±0.28	4.28±0.43	5.20±0.47	4.37±0.44	FA > O_3
5.86±0.66	5.38±0.36	5.28±0.37	4.66±0.27	5.19±0.37	4.31±0.44	6.01±0.61	4.71±0.54	FA > O_3
2.67±0.34	2.18±0.15	2.35±0.16	2.17±0.36	2.13±0.13	2.15±0.35	2.74±0.25	2.60±0.67	FA > O_3
1.80±0.23	2.22±0.31	1.68±0.15	2.02±0.15	1.79±0.10	2.18±0.26	1.75±0.14	2.09±0.14	
224±12	214±10	227±10	207±15	214±7	202±10	221±8	195±7	Pre > Post

Continued from page 21

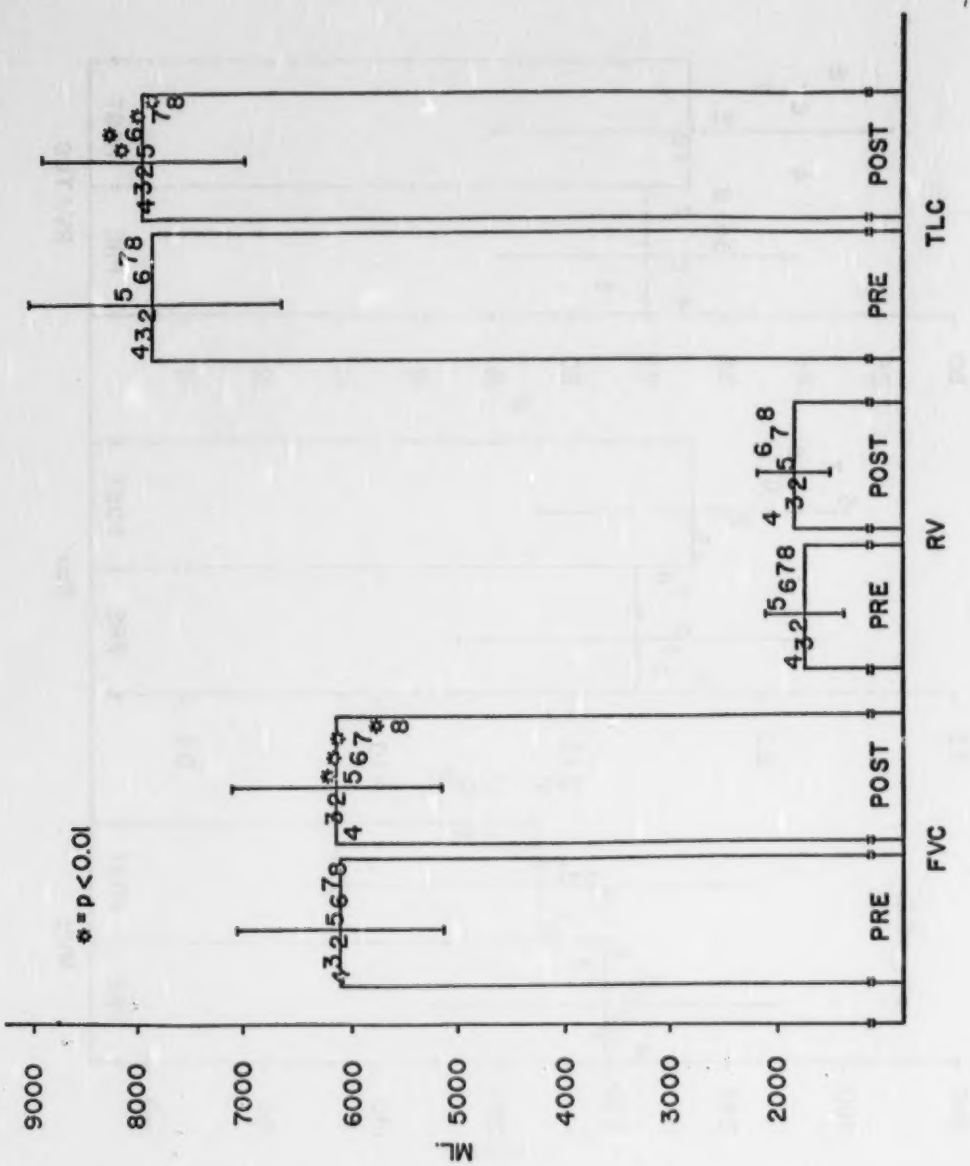

FIGURE 1a.

Pre- and post-exposure values for FVC, RV, and TLC for all eight ambient conditions. The histograms represent the mean (±SE) for condition 1 (FA, 25°C), while the numerals indicate the mean values for the remaining seven conditions. Numbers 2, 3, and 4 on the left of the SE bar are filtered air environments, while 5, 6, 7, and 8 on the right of the SE bar are equivalent ambient environments with 0.5 ppm ozone.

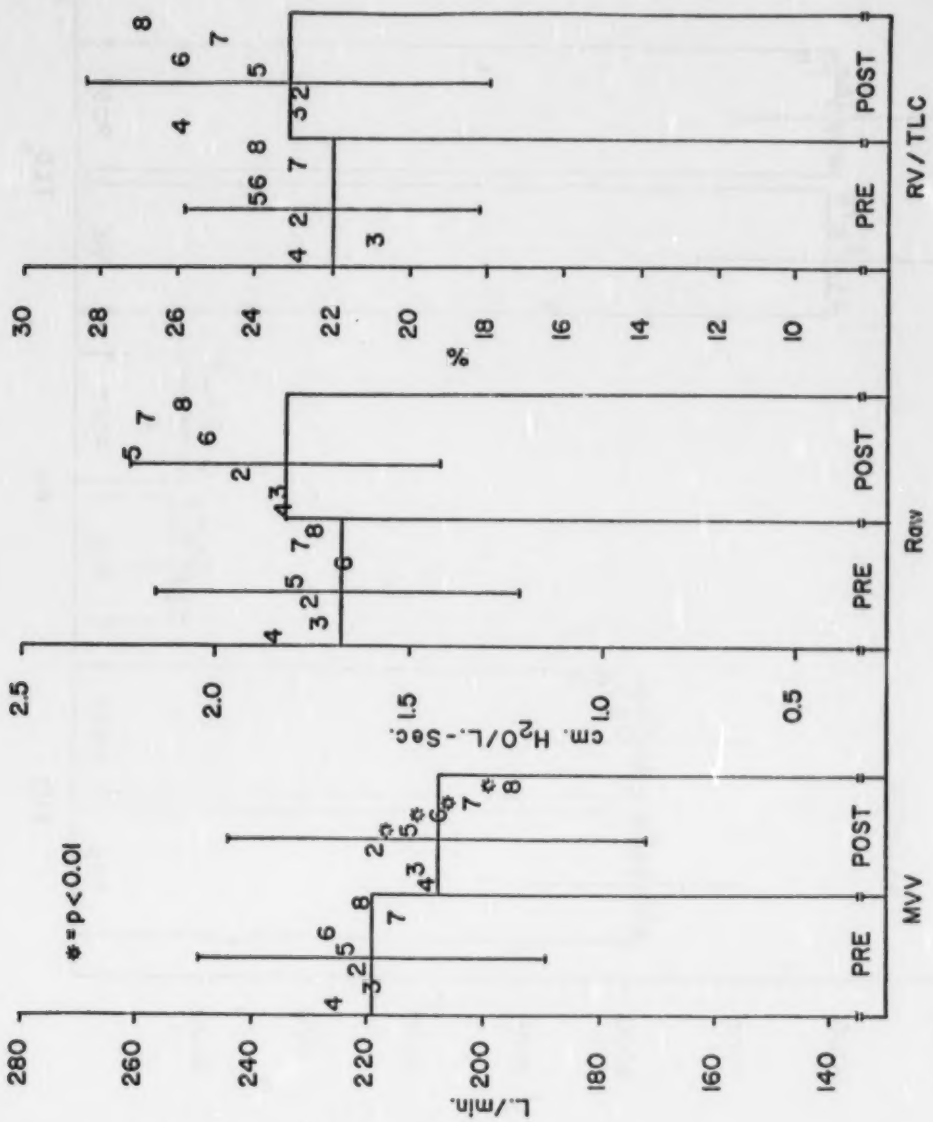

FIGURE 1b.

Pre- and post-exposure values for IC, ERV, and FRC for all eight ambient conditions. The histograms represent the mean (±SE) for condition 1 (FA, 25°C), while the numerals indicate the mean values for the remaining seven conditions. Numbers 2, 3, and 4 on the left of the SE bar are filtered air environments, while 5, 6, 7, and 8 on the right of the SE bar are equivalent ambient environments with 0.5 ppm ozone.

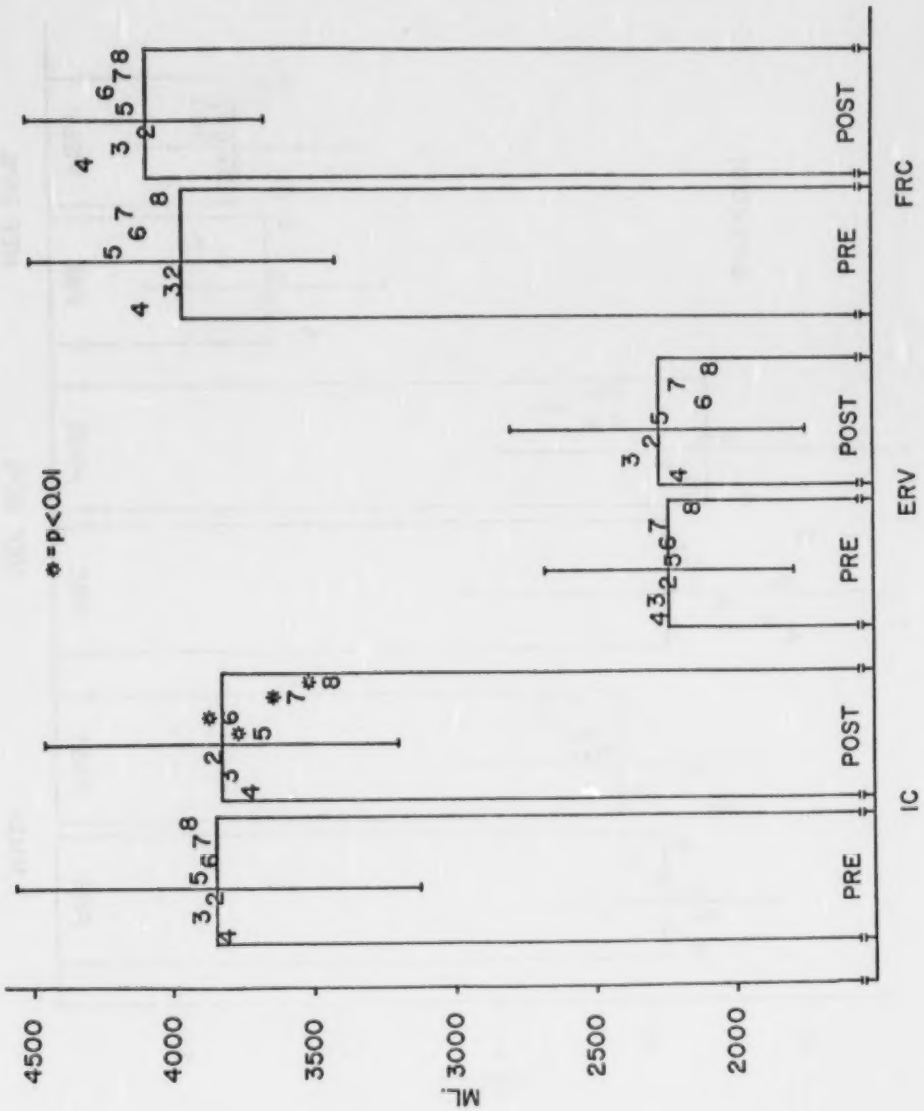

FIGURE 1c.

Pre- and post-exposure values for MVV, R_{aw}, and RV/TLC for all eight ambient conditions. The histograms represent the mean (±SE) for condition 1 (FA, 25°C), while the numerals indicate the mean values for the remaining seven conditions. Numbers 2, 3, and 4 on the left of the SE bar are filtered air environments, while 5, 6, 7, and 8 on the right of the SE bar are equivalent ambient environments with 0.5 ppm ozone.

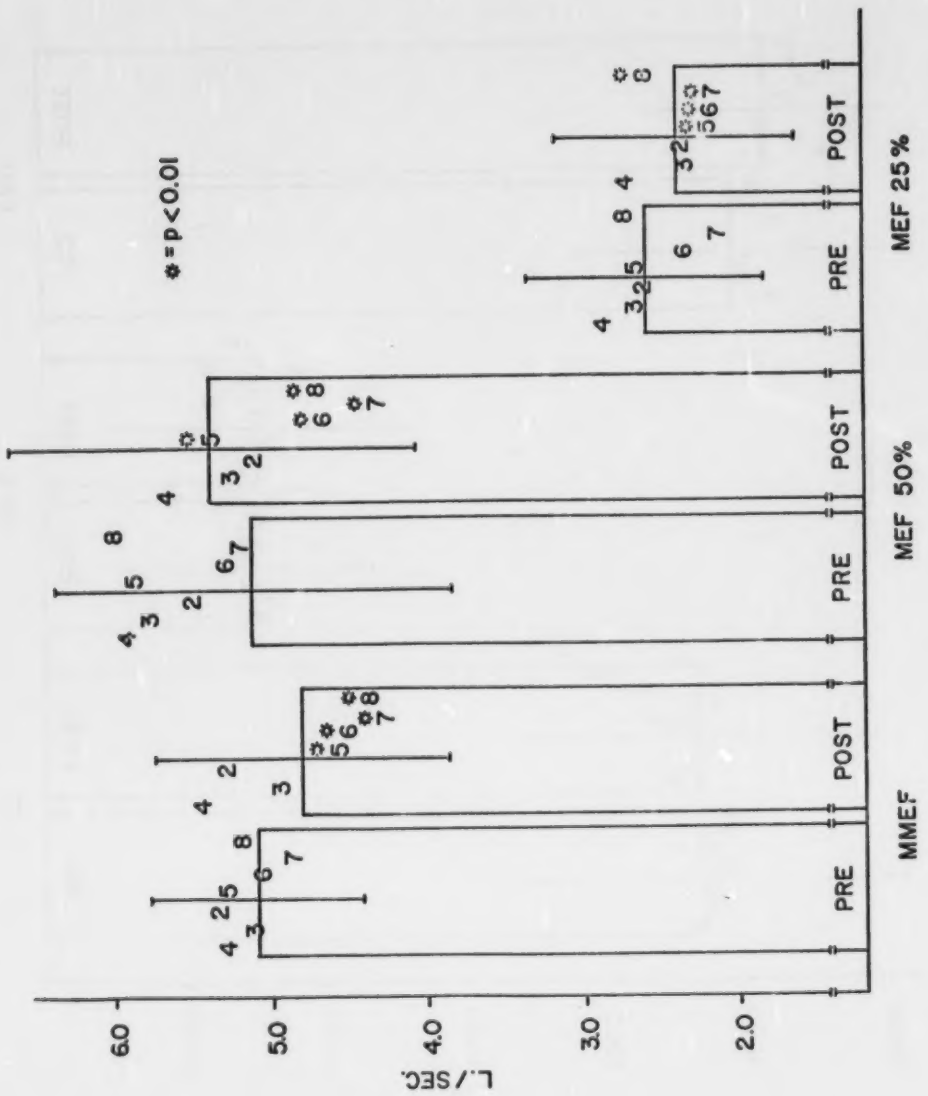

FIGURE 1d.

Pre- and post-exposure values for MMEF, MEF50%, and MEF25% for all eight ambient conditions. The histograms represent the mean (±SE) for condition 1 (FA, 25°C), while the numerals indicate the mean values for the remaining seven conditions. Numbers 2, 3, and 4 on the left of the SE bar are filtered air environments, while 5, 6, 7, and 8 on the right of the SE bar are equivalent ambient environments with 0.5 ppm ozone.

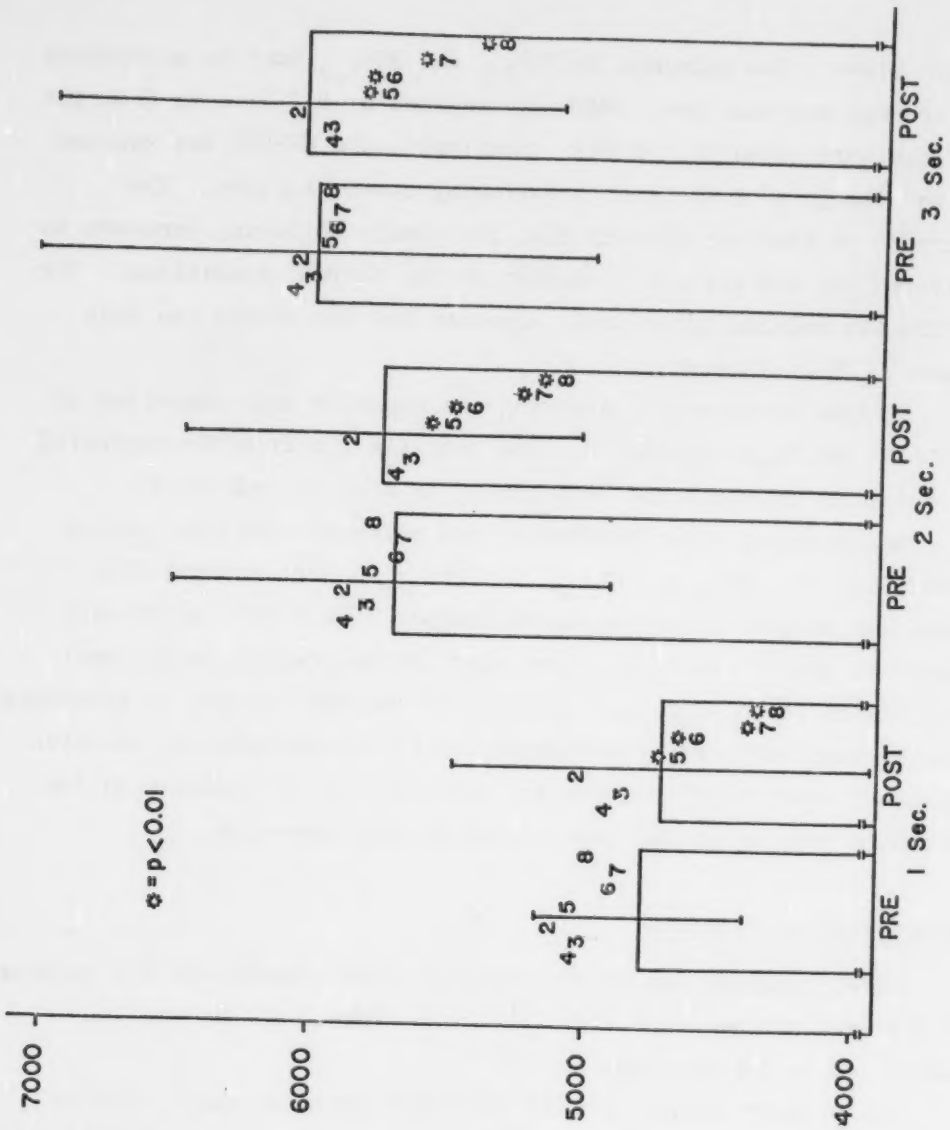

FIGURE 1e.

FIGURE 1e.

Pre- and post-exposure values for $FEV_{1.0}$, $FEV_{2.0}$, and $FEV_{3.0}$ for all eight ambient conditions. The histograms represent the mean (±SE) for condition 1 (FA, 25°C), while the numerals indicate the mean values for the remaining seven conditions. Numbers 2, 3, and 4 on the left of the SE bar are filtered air environments, while 5, 6, 7, and 8 on the right of the SE bar are equivalent ambient environments with 0.5 ppm ozone.

basis alone. The decrease in $FEV_{2.0}$ and $FEV_{1.0}$ must be attributed to reduced maximum flow. MMEF was reduced by 0.7 liter/s from the pre-exposure value ($P < 0.05$). Similarly, the MEF50% was reduced by an average of 0.85 liter/s following ozone exposure. The decrease in flow was greater than the change following exposure to filtered air and was not dependent on the thermal conditions. The MEF25% was reduced after ozone exposure but the change was less dramatic (0.16 liter/s).

Changes which occurred during the exposure are summarized in Table 5* and Figs. 2a and 2b. The time (in min from the beginning of exposure) at which the measurement is made is indicated.

Measurements made immediately following the exercise period (100 min) — VC, $FEV_{1.0}$, $FEV_{2.0}$, and $FEV_{3.0}$ — were reduced when ozone was present in the exposure chamber (Table 6). MEF25% was higher in code 4 and code 8 (the most severe thermal conditions). This effect may be due to a decrease of the ERV because of faintness felt by some subjects; a prolonged expiratory maneuver (a Valsalva maneuver) would tend to aggravate any problems of hypotension due to venous pooling in the legs caused by heat exposure.

Cardiovascular Function

Cardiovascular and metabolic alterations during the 2-h exposure to filtered air or ozone under the four thermal conditions are summarized in Tables 7 and 8.

The primary change in cardiovascular function was a rise in exercise heart rate at higher ambient temperatures (B4 > B2, B3 > B1). This was accompanied by a decline in stroke volume (B1 > B4) as cardiac output+ in the heat was not significantly altered by temperature or ozone exposure. Stroke index, cardiac index, or $(a - v)O_2$ difference were neither affected by temperature nor ozone exposure.

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*See Appendix C for a discussion of closing volume data for this time period.

+Cardiac output and stroke volume values are not presented but can be calculated from the mean BSA (1.97) and mean heart rate (Table 8) using the value given for cardiac index (CI = CO/BSA).

Table 5. PULMONARY FUNCTION CHANGES DURING 2-HOUR EXPOSURE TO FILTERED AIR OR 0.5 ppm OZONE AT VARIOUS AMBIENT ENVIRONMENTAL CONDITIONS[a,b]

	Time,[c] min	FVC, ml	$FEV_{1.0}$, ml	$FEV_{2.0}$, ml	$FEV_{3.0}$, ml	MMEF, liters/sec	MEF50%, liters/sec	MEF25% liters/sec
CODE 1	12.5	6035±376	4478±239	5359±252	5555±276	4.55±0.61	5.52±0.75	2.74±0.42
	27.5	6252±416	4622±185	5642±244	6035±340	4.71±0.53	5.19±0.56	2.46±0.35
	57.5	6166±369	4558±183	5624±219	5995±306	4.19±0.53	5.23±0.48	2.22±0.32
	100.0	6127±391	4613±195	5612±259	5936±349	4.39±0.46	5.09±0.65	2.29±0.26
	117.5	6202±410	4753±136	5740±352	6010±451	4.63±0.47	5.33±0.49	2.47±0.33
CODE 2	12.5	6287±396	5140±203	5960±342	6244±408	5.35±0.26	6.68±0.34	2.79±0.32
	27.5	6214±414	4797±153	5759±264	6098±347	5.09±0.46	6.17±0.47	2.79±0.18
	57.5	6188±422	4987±147	5912±365	6212±442	5.03±0.32	5.86±0.35	2.75±0.30
	100.0	6064±400	4741±138	5766±258	5992±332	4.56±0.34	5.11±0.46	2.48±0.31
	117.5	6243±411	5008±214	6006±339	6225±410	5.09±0.22	5.46±0.60	2.68±0.31
CODE 3	12.5	6393±441	4782±109	5773±246	6180±419	4.39±0.35	5.99±0.47	2.63±0.40
	27.5	6308±433	5069±363	6023±466	6242±485	5.40±0.52	6.17±0.67	3.02±0.31
	57.5	6227±442	4870±133	5773±398	6066±548	4.79±0.58	5.60±0.64	2.89±0.42
	100.0	6217±413	4888±144	5792±328	6124±419	4.84±0.34	5.63±0.43	2.56±0.26
	117.5	6474±438	5068±61	6167±336	6482±391	4.74±0.38	5.68±0.60	2.80±0.29
CODE 4	12.5	6145±411	4865±242	5593±291	5776±326	5.01±0.56	6.46±0.72	2.93±0.50
	27.5	6143±391	4802±236	5543±330	5735±345	5.18±0.49	6.12±0.48	3.16±0.60
	57.5	6033±411	4849±235	5665±371	5948±440	5.11±0.58	6.45±0.68	3.08±0.77
	100.0	5478±405	4691±232	5261±377	5425±433	5.64±0.69	6.48±0.81	3.10±0.54
	117.5	5876±408	4608±229	5191±348	5472±408	5.25±0.53	6.05±0.57	2.99±0.57

[d] MEF25% higher in codes 4 and 8 than in all others.

[a] Subjects walked at approximately 40% $\dot{V}_{O_2\ max}$ from 60-90 minutes.

[b] Underlined values are significantly reduced ($P<0.10$) in ozone exposures at this time (immediately post-exercise).

[c] Time is elapsed time in minutes from the beginning of ozone exposure.

(Continued on next page.)

Table 5 (continued). PULMONARY FUNCTION CHANGES DURING 2-HOUR EXPOSURE TO FILTERED AIR OR 0.5 ppm OZONE AT VARIOUS AMBIENT ENVIRONMENTAL CONDITIONS[a,b]

	Time,[c] min	FVC, ml	$FEV_{1.0}$, ml	$FEV_{2.0}$, ml	$FEV_{3.0}$, ml	MMEF, liters/sec	MEF50%, liters/sec	MEF25% liters/sec
CODE 5	12.5	6212±366	4849±246	5763±306	5997±351	4.92±0.36	5.59±0.48	2.55±0.24
	27.5	6130±416	4734±241	5703±333	5959±414	4.48±0.37	5.36±0.46	2.41±0.35
	57.5	6215±401	4705±202	5762±320	6016±387	4.61±0.43	5.29±0.48	2.65±0.40
	100.0	5991±392	4541±215	5459±318	5740±382	4.30±0.32	4.93±0.32	2.36±0.42
	117.5	5945±386	4437±277	5383±349	5708±394	4.11±0.44	4.79±0.51	2.45±0.40
CODE 6	12.5	5955±274	4639±236	5539±239	5776±248	4.71±0.41	5.40±0.48	2.40±0.25
	27.5	5985±316	4597±202	5533±260	5768±291	4.67±0.40	5.61±0.51	2.84±0.55
	57.5	5977±302	4599±231	5527±268	5730±292	4.66±0.40	5.35±0.49	2.49±0.28
	100.0	5756±355	4207±165	5150±277	5494±332	3.99±0.38	4.50±0.39	2.07±0.27
	117.5	5896±411	4349±162	5354±301	5675±383	4.25±0.34	4.75±0.34	2.27±0.26
CODE 7	12.5	6222±396	4770±290	5725±402	6004±400	4.88±0.52	5.59±0.47	2.70±0.48
	27.5	6146±472	4464±214	5674±426	5955±467	4.49±0.44	5.43±0.54	2.40±0.24
	57.5	6167±430	4503±223	5422±235	5632±246	4.44±0.44	5.21±0.51	2.56±0.32
	100.0	5564±443	4270±329	5056±417	5291±454	4.35±0.68	4.90±0.61	2.32±0.51
	117.5	5838±414	4325±256	5244±307	5528±350	4.10±0.54	4.55±0.33	1.91±0.30
CODE 8	12.5	6158±385	4604±236	5577±312	5903±403	4.79±0.53	5.40±0.66	2.34±0.42
	27.5	6187±369	4846±216	5568±391	5696±358	5.29±0.51	5.46±0.63	2.70±0.41
	57.5	6229±395	4555±381	5698±374	6004±399	4.66±0.47	5.19±0.54	2.83±0.40
	100.0	5474±354	4174±244	5036±289	5480±285	4.11±0.43	4.52±0.53	2.57±0.50
	117.5	5782±275	4396±205	5289±270	5576±287	4.26±0.36	5.34±0.56	2.54±0.41

[d]

[a] Subjects walked at approximately 40% $\dot{V}_{O_2\ max}$ from 60-90 minutes.

[b] Underlined values are significantly reduced ($P<0.10$) in ozone exposures at this time (immediately post-exercise).

[c] Time is elapsed time in minutes from the beginning of ozone exposure.

[d] MEF25% higher in codes 4 and 8 than in all others.

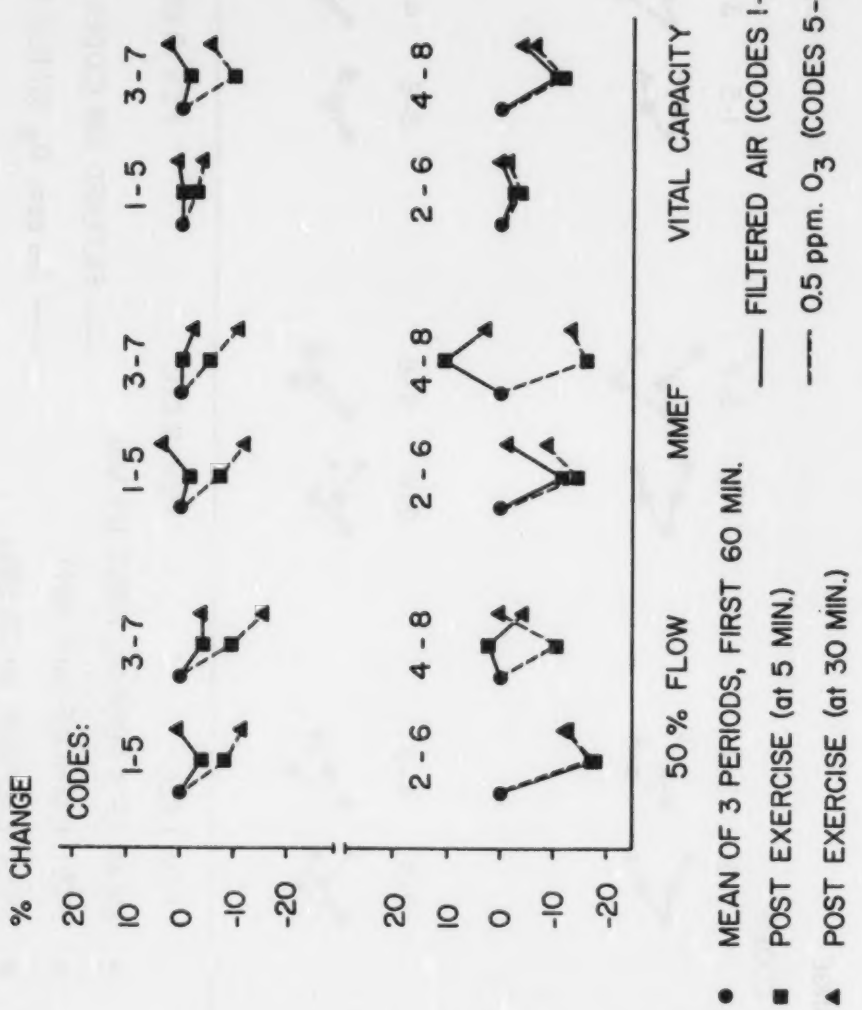

FIGURE 2a.

Percent change in VC, MEF50%, and MMEF in all eight ambient conditions as affected by a 30-min period of exercise. There were no significant differences in the first hour and these values were averaged for the comparisons after the exercise period.

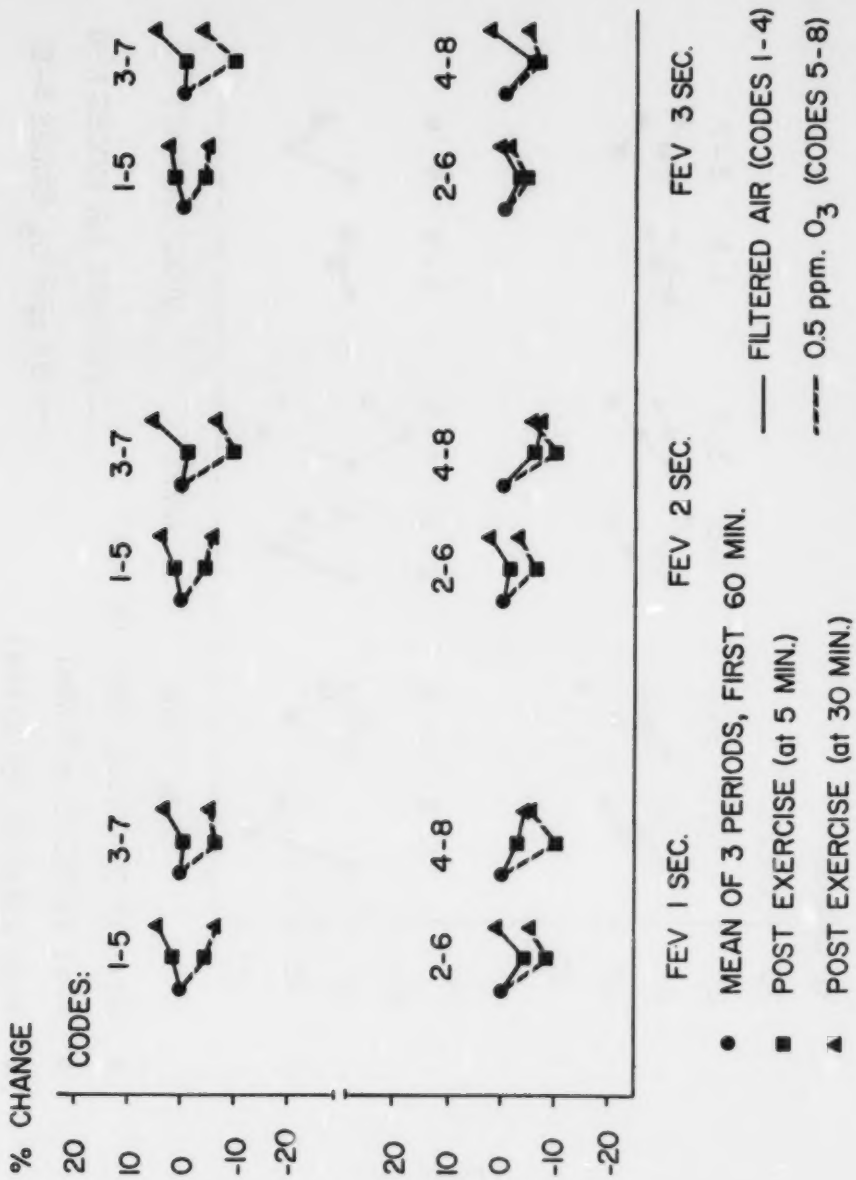

FIGURE 2b.

Percent change in $FEV_{1.0}$, $FEV_{2.0}$, and $FEV_{3.0}$ in all eight ambient conditions as affected by a 30-min period of exercise. There were no significant differences in the first hour and these values were averaged for the comparisons after the exercise period.

Table 6. PULMONARY FUNCTION CHANGES FOLLOWING EXERCISE AND AT END-EXPOSURE

		Period 1	Period 4	Period 8	$\bar{X}$[a]	Period 16	% change[b] (P. 16)	Period 18	% change[b] (P. 18)
CODE 1	VC, ml	6034	6252	6166	6143	6127	-0.26	6202	+0.96
	$FEV_{1.0}$, ml	4478	4622	4558	4552	4613	+1.33	4752	+4.39
	$FEV_{2.0}$, ml	5359	5641	5625	5542	5612	+1.27	5740	+3.57
	$FEV_{3.0}$, ml	5555	6035	5995	5795	5937	+2.45	6010	+3.71
	MEF50%, liters/sec	5.52	5.19	5.23	5.31	5.09	-2.32	5.33	+0.38
	MMEF, liters/sec	4.55	4.71	4.19	4.48	4.39	-2.08	4.63	+3.35
CODE 2	VC, ml	6287	6214	6188	6230	6064	-2.66	6242	+0.19
	$FEV_{1.0}$, ml	5140	4797	4987	4975	4741	-4.70	5008	+0.66
	$FEV_{2.0}$, ml	5960	5759	5912	5877	5766	-1.89	6006	+2.19
	$FEV_{3.0}$, ml	6244	6098	6212	6185	5992	-3.12	6225	+0.65
	MEF50%, liters/sec	6.68	6.17	5.86	6.24	5.11	-18.1	5.46	-12.5
	MMEF, liters/sec	5.35	5.09	5.03	5.16	4.56	-11.6	5.09	-1.36
CODE 3	VC, ml	6393	6308	6226	6309	6216	-1.47	6474	+2.62
	$FEV_{1.0}$, ml	4782	5069	4870	4907	4888	-0.39	5068	+3.28
	$FEV_{2.0}$, ml	5773	6023	5773	5856	5792	-1.09	6167	+5.31
	$FEV_{3.0}$, ml	6180	6242	6066	6163	6124	-0.63	6482	+5.18
	MEF50%, liters/sec	5.99	6.17	5.60	5.92	5.63	-4.90	5.68	-4.05
	MMEF, liters/sec	4.39	5.40	4.79	4.86	4.84	-0.41	4.74	-2.47
CODE 4	VC, ml	6144	6142	6034	6107	5478	-10.30	5876	-3.78
	$FEV_{1.0}$, ml	4865	4802	4849	4839	4691	-3.06	4608	-4.77
	$FEV_{2.0}$, ml	5593	5543	5665	5600	5261	-6.05	5191	-7.30
	$FEV_{3.0}$, ml	5776	5735	5948	5820	5470	-6.01	5963	+2.46
	MEF50%, liters/sec	6.46	6.12	6.45	6.34	6.48	+2.21	6.05	-4.57
	MMEF, liters/sec	5.01	5.18	5.11	5.10	5.64	+10.59	5.25	+2.94

[a] $\bar{X}$ indicates mean value for periods 1-4.

[b] Percent change is indicated for post-exercise period (P. 16) and end-exposure period (P. 18).

(Continued on next page.)

Table 6 (continued). PULMONARY FUNCTION CHANGES FOLLOWING EXERCISE AND AT END-EXPOSURE

		Period 1	Period 4	Period 8	$\bar{X}$[a]	Period 16	% change[b] (P. 16)	Period 18	% change[b] (P. 18)
CODE 5	VC, ml	6212	6130	6215	6186	5991	-3.15	5945	-3.90
	$FEV_{1.0}$, ml	4849	4734	4705	4763	4541	-4.66	4437	-6.84
	$FEV_{2.0}$, ml	5763	5703	5762	5743	5459	-4.94	5384	-6.25
	$FEV_{3.0}$, ml	5997	5959	6016	5991	5740	-4.19	5708	-4.72
	MEF50%, liters/sec	5.59	5.36	5.29	5.41	4.93	-8.87	4.79	-11.46
	MMEF, liters/sec	4.92	4.48	4.61	4.67	4.30	-7.92	4.11	-11.99
CODE 6	VC, ml	5955	5985	5977	5972	5756	-3.62	5896	-1.27
	$FEV_{1.0}$, ml	4639	4597	4599	4612	4207	-8.78	4349	-5.70
	$FEV_{2.0}$, ml	5539	5533	5527	5533	5150	-6.92	5354	-3.24
	$FEV_{3.0}$, ml	5776	5768	5730	5758	5494	-4.58	5675	-1.44
	MEF50%, liters/sec	5.40	5.61	5.35	5.45	4.50	-17.43	4.75	-12.84
	MMEF, liters/sec	4.71	4.67	4.66	4.68	3.99	-14.74	4.25	-9.19
CODE 7	VC, ml	6222	6146	6167	6178	5564	-9.94	5838	-5.50
	$FEV_{1.0}$, ml	4770	4464	4503	4579	4270	-6.75	4325	-5.55
	$FEV_{2.0}$, ml	5725	5674	5422	5607	5056	-9.83	5244	-6.47
	$FEV_{3.0}$, ml	6004	5955	5632	5864	5291	-9.77	5660	-3.48
	MEF50%, liters/sec	5.59	5.43	5.21	5.41	4.90	-9.43	4.55	-15.90
	MMEF, liters/sec	4.88	4.49	4.44	4.60	4.35	-5.43	4.10	-10.87
CODE 8	VC, ml	6158	6187	6229	6191	5474	-11.58	5782	-6.61
	$FEV_{1.0}$, ml	4604	4846	4555	4668	4174	-10.58	4396	-5.83
	$FEV_{2.0}$, ml	5577	5568	5698	5614	5036	-10.30	5289	-5.79
	$FEV_{3.0}$, ml	5903	5696	6004	5868	5480	-6.61	5576	-4.98
	MEF50%, liters/sec	5.40	5.46	5.19	5.35	4.52	-15.51	5.34	-0.19
	MMEF, liters/sec	4.79	5.29	4.66	4.91	4.11	-16.29	4.26	-13.24

[a] $\bar{X}$ indicates mean value for periods 1-4.

[b] Percent change is indicated for post-exercise period (P. 16) and end-exposure period (P. 18).

Table 7. PERIPHERAL BLOOD FLOW (ml/100 ml/min) DURING EXPOSURE TO FILTERED AIR OR 0.5 ppm OZONE AT VARIOUS AMBIENT ENVIRONMENTAL TEMPERATURES

Period	Code 1 (FA)	Code 5 (O^3)	Code 2 (FA)	Code 6 (O^3)	Code 3 (FA)	Code 7 (O^3)	Code 4 (FA)	Code 8 (O^3)
			MEAN FOREARM FLOW					
1	1.81	1.88	3.92	3.60	2.50	2.15	3.29	3.76
3	2.34	2.46	3.20	2.59	2.72	2.46	3.43	4.53
5	1.61	2.72	3.21	3.10	2.68	2.19	4.56	3.88
8	1.75	2.27	3.68	2.65	3.83	2.37	4.02	4.56
15[a]	1.91	2.48	4.74	4.43	5.58	3.32	5.89	7.79
18	2.19	2.30	4.64	3.42	4.35	2.34	7.51	7.57
			MEAN HAND AND FOREARM FLOW					
1	1.37	1.97	3.72	2.63	2.51	2.11	3.77	2.49
3	1.74	1.56	4.59	3.65	3.19	2.79	4.08	2.93
5	1.77	1.15	3.53	3.38	4.19	3.90	5.46	4.58
8	1.71	2.44	4.35	3.31	4.41	3.25	3.67	3.86
15[a]	3.50	2.67	5.61	4.57	3.53	2.97	5.30	--
18	1.43	2.12	3.97	4.76	7.15	4.03	5.61	3.82

[a] Post-exercise (exercise period 30 minutes duration).

Table 8. METABOLIC AND CARDIOVASCULAR CHANGES DURING EXPOSURE TO FILTERED AIR OR 0.5 ppm OZONE FOR 2 HOURS

	Time, min	$\dot{V}_{BTPS}$, liters/min	$\dot{V}_{alveol.}$, liters/min	RR, breaths/min	O_2 uptake, liters/min STPD	% $\dot{V}O_2$ max	R	O_2 pulse	CI, liters/min·m^2	HR, beats/min
CODE 1	3	9.74±0.74	6.16±0.53	16.6±1.1	0.30±0.02	0.08±0.01	0.83±0.02	4.06±0.27	2.93±0.31	74.2±3.7
	48	9.32±1.23	5.67±0.93	15.5±1.6	0.28±0.04	0.07±0.01	0.80±0.02	3.84±0.40	2.03±0.11	73.6±5.2
	83[a]	35.95±1.19	27.66±1.21	21.4±1.8	1.44±0.06	0.38±0.02	0.88±0.02	12.22±0.80	8.07±0.84	119.0±4.4
	108	9.50±0.88	6.05±0.67	16.4±1.7	0.30±0.03	0.08±0.01	0.80±0.02	3.97±0.24	2.75±0.30	74.4±3.7
CODE 2	3	9.75±0.55	6.10±0.48	16.6±1.1	0.31±0.01	0.08±0.01	0.80±0.02	4.12±0.21	2.98±0.21	75.5±3.2
	48	9.28±0.66	6.03±0.64	15.5±1.7	0.29±0.02	0.08±0.01	0.80±0.03	3.67±0.29	2.66±0.28	79.9±3.1
	83[a]	36.58±0.98	30.21±1.22	24.6±2.8	1.45±0.02	0.39±0.02	0.90±0.02	11.19±0.36	8.78±0.48	130.4±3.2
	108	9.87±0.63	6.64±0.64	16.6±1.6	0.30±0.02	0.08±0.01	0.83±0.04	3.62±0.28	2.81±0.24	85.2±4.1
CODE 3	3	10.13±0.91	6.56±0.71	15.6±1.5	0.32±0.02	0.09±0.01	0.81±0.03	3.86±0.31	3.51±0.33	84.6±5.9
	48	9.49±0.84	6.28±0.68	15.8±1.9	0.28±0.02	0.07±0.00	0.87±0.04	3.32±0.36	2.82±0.27	86.1±5.2
	83[a]	36.17±1.15	30.33±1.40	22.9±2.4	1.42±0.03	0.38±0.02	0.92±0.02	11.00±0.48	8.85±0.58	130.4±5.4
	108	10.30±0.52	6.69±0.43	17.6±1.8	0.30±0.02	0.08±0.01	0.86±0.03	3.55±0.38	3.38±0.38	89.4±7.5
CODE 4	3	10.27±1.41	6.85±1.45	17.8±1.7	0.31±0.03	0.08±0.01	0.82±0.02	3.55±0.33	2.76±0.26	86.2±4.1
	48	11.35±1.70	7.57±1.56	18.6±1.0	0.32±0.04	0.09±0.01	0.81±0.04	3.64±0.42	2.94±0.36	88.9±4.6
	83[a]	40.32±2.72	32.40±3.23	27.6±4.8	1.55±0.08	0.42±0.02	0.88±0.02	10.53±0.73	9.43±0.45	149.6±8.0
	108	15.13±4.03	11.38±3.47	19.5±2.3	0.39±0.06	0.10±0.02	0.84±0.03	3.44±0.47	2.89±0.28	111.2±5.8
CODE 5	3	8.48±0.62	5.24±0.59	13.6±1.5	0.26±0.02	0.07±0.01	0.79±0.03	3.83±0.25	2.76±0.33	69.2±4.4
	48	8.87±0.78	5.60±0.66	14.4±1.9	0.26±0.02	0.07±0.01	0.85±0.03	3.73±0.22	2.96±0.31	69.1±4.0
	83[a]	33.33±1.68	27.82±1.79	22.6±2.4	1.32±0.04	0.35±0.02	0.92±0.03	11.43±0.68	8.33±0.79	116.5±4.2
	108	8.74±0.53	5.39±0.40	16.4±1.4	0.26±0.02	0.07±0.01	0.83±0.03	3.05±0.29	2.79±0.17	83.9±4.9
CODE 6	3	9.72±0.86	5.82±0.59	14.9±1.1	0.28±0.02	0.07±0.00	0.81±0.03	3.54±0.35	2.64±0.25	80.0±4.0
	48	10.48±1.15	6.71±1.17	15.8±2.1	0.29±0.02	0.08±0.01	0.83±0.03	3.51±0.29	2.72±0.33	83.2±5.0
	83[a]	35.21±2.11	29.45±2.21	23.9±3.4	1.43±0.07	0.38±0.02	0.89±0.03	10.49±0.82	8.29±0.53	137.9±4.3
	108	11.48±1.14	7.71±0.87	18.6±3.0	0.33±0.03	0.09±0.01	0.85±0.04	3.55±0.44	2.87±0.30	94.8±5.5
CODE 7	3	9.49±1.10	6.15±0.96	15.9±3.4	0.26±0.02	0.07±0.00	0.89±0.04	3.48±0.37	2.48±0.19	77.4±4.7
	48	10.43±1.35	6.70±1.17	19.1±3.1	0.28±0.03	0.08±0.01	0.89±0.05	3.49±0.32	2.58±0.25	80.4±4.2
	83[a]	34.19±2.12	28.77±2.25	29.5±6.0	1.31±0.09	0.35±0.02	0.92±0.03	10.36±0.79	7.64±0.54	127.4±4.4
	108	9.78±0.77	6.66±0.82	20.6±4.8	0.30±0.03	0.08±0.01	0.83±0.03	3.53±0.33	2.78±0.19	86.4±2.9
CODE 8	3	9.74±0.96	6.27±0.73	14.9±0.9	0.29±0.02	0.08±0.01	0.83±0.04	3.68±0.38	2.73±0.23	82.8±7.8
	48	9.95±1.50	6.60±1.34	13.4±1.6	0.29±0.02	0.08±0.01	0.81±0.05	3.27±0.20	3.08±0.23	88.6±6.2
	83[a]	39.12±1.40	32.01±1.43	28.9±6.0	1.45±0.06	0.39±0.02	0.92±0.01	9.62±0.69	8.57±0.60	153.4±7.2
	108	14.78±1.69	9.95±1.59	18.0±1.7	0.39±0.04	0.10±0.01	0.86±0.04	3.49±0.43	3.79±0.44	113.7±9.2

[a] Subjects walked at approximately 40% $\dot{V}O_2$ max from 60-90 minutes.

(Continued on page 37)

(Continued from page 36)

Table 8. (Continued)

Blood pressure, torr		TPR, dyn·sec cm^{-5}	CW, kg·m/min	Index of left ventricular function (SPxHRx10^3)	$D_{L_{CO}}$	$\dot{V}_A/\dot{Q}$	Diff. Perf.	T_{re}, °C	$\bar{T}_b$, °C	Tissue conductance, kcal/ m^2·h^{-1}·°C^{-1}
Systolic	Diastolic									
120±5	81.0±3.2	1386±145	9.52±1.75	9.32±1.03	18.0±1.5	1.13±0.14	3.16±0.33	37.3±0.1	35.4±0.1	8.2±0.5
120±4	85.2±4.4	1937±178	6.56±0.25	8.73±1.13	22.7±3.3	1.37±0.43	4.79±0.93	37.2±0.1	35.4±0.1	8.3±0.9
133±6	71.2±1.7	496±117	29.91±7.59	1.68±0.68	51.1±3.7	1.77±0.15	3.25±0.32	37.6±0.1	35.7±0.2	41.3±2.5
120±3	80.0±3.2	1426±191	9.06±1.31	8.92±0.61	19.6±2.6	1.15±0.16	3.77±0.46	37.6±0.1	36.0±0.1	9.9±1.2
117±4	81.2±2.3	1337±152	9.28±0.69	9.35±0.78	19.7±2.7	1.09±0.16	3.17±0.41	37.3±0.2	35.9±0.2	12.0±0.5
122±4	85.6±2.4	1492±180	9.28±1.19	9.89±0.59	22.2±3.2	1.24±0.18	4.30±0.64	37.2±0.2	36.2±0.2	15.3±1.7
131±3	78.1±2.7	463±16	29.68±1.65	17.32±0.88	52.0±5.7	1.80±0.18	2.97±0.41	37.7±0.1	36.5±0.1	68.6±4.4
119±4	83.3±2.9	1374±169	9.47±1.05	10.62±0.76	24.4±5.4	1.26±0.18	4.59±0.85	37.8±0.1	36.6±0.1	13.3±1.3
119±2	79.2±2.2	1153±134	10.86±0.94	9.58±0.46	20.9±1.5	0.95±0.11	3.11±0.32	37.2±0.1	36.2±0.1	16.4±1.4
119±3	82.1±3.5	1436±129	8.87±0.80	9.82±0.42	22.2±2.2	1.17±0.12	4.08±0.36	37.2±0.1	36.4±0.1	19.1±1.6
138±6	70.7±4.3	455±45	31.47±1.51	17.90±1.18	48.6±2.5	1.80±0.15	2.88±0.22	37.7±0.1	36.8±0.1	82.8±5.9
118±3	82.7±2.1	1231±174	10.65±1.26	10.85±0.88	21.3±1.4	1.13±0.13	3.55±0.47	37.8±0.1	36.7±0.1	16.2±2.0
116±3	81.1±2.8	1474±214	8.02±0.82	9.90±0.47	22.3±2.6	1.43±0.50	4.42±0.54	37.1±0.1	36.2±0.2	19.4±2.9
116±4	83.2±2.0	1459±196	9.03±1.12	10.76±0.65	22.8±2.3	1.52±0.40	4.26±0.55	37.2±0.1	36.6±0.1	28.3±5.8
138±5	78.2±9.5	434±63	34.69±1.21	21.07±0.87	53.2±6.1	1.81±0.24	3.04±0.54	37.8±0.1	37.1±0.2	141.8±34.1
112±4	77.3±2.3	1355±204	8.71±1.12	12.09±0.56	30.9±3.4	2.16±0.69	6.11±1.13	38.0±0.1	37.2±0.2	29.8±7.9
115±2	78.8±3.0	1444±198	8.30±0.99	8.44±0.75	22.2±1.6	1.10±0.27	4.17±0.52	37.2±0.2	35.4±0.2	7.8±0.7
116±4	79.8±2.0	1351±136	9.17±1.04	8.02±0.60	20.4±1.7	1.04±0.20	3.40±0.39	37.1±0.1	35.5±0.1	8.5±1.0
134±4	77.3±3.3	480±111	30.64±5.06	16.54±0.64	49.4±2.6	1.85±0.26	2.85±0.29	37.5±0.1	35.8±0.1	42.4±3.2
117±4	77.8±2.3	1356±83	8.80±0.79	9.35±0.95	22.2±1.7	1.01±0.10	4.06±0.42	37.5±0.1	36.0±0.1	9.1±0.8
113±3	83.2±2.5	1519±150	8.00±0.85	8.94±0.64	19.5±3.2	1.26±0.25	3.98±0.97	37.2±0.1	36.0±0.1	11.2±0.8
114±4	84.0±5.1	1522±191	8.16±0.90	9.32±0.82	16.1±2.0	1.29±0.30	2.88±0.57	37.2±0.1	36.2±0.1	14.7±1.1
134±5	74.4±8.6	427±18	32.06±0.71	17.91±1.01	48.4±5.9	1.82±0.23	3.02±0.47	37.7±0.1	36.6±0.1	68.8±3.6
114±3	81.9±4.4	1343±139	9.05±1.05	11.08±1.10	18.4±3.5	1.48±0.26	3.57±0.76	37.8±0.1	36.7±0.1	15.5±1.2
121±3	82.2±2.3	1602±148	8.21±0.81	9.46±0.55	20.9±3.5	1.32±0.23	4.58±0.94	37.1±0.1	36.0±0.1	12.3±1.1
116±3	81.2±2.0	1540±122	7.95±0.71	9.50±0.57	22.2±2.8	1.37±0.25	4.54±0.59	37.1±0.1	36.2±0.1	17.0±1.9
127±2	70.0±6.0	461±69	28.00±2.37	15.63±0.78	52.7±5.0	1.94±0.28	3.37±0.43	37.5±0.1	36.6±0.1	77.7±6.8
114±3	78.9±2.6	1354±71	8.69±0.69	9.84±0.50	19.8±2.9	1.32±0.22	3.85±0.71	37.6±0.1	36.6±0.1	14.8±1.3
119±4	84.6±3.8	1482±162	8.84±0.91	10.61±0.87	21.1±2.5	1.17±0.08	4.07±0.56	37.2±0.2	36.3±0.2	17.8±1.6
119±4	84.9±3.2	1313±99	9.77±0.85	11.15±1.09	18.6±1.7	1.16±0.30	3.12±0.24	37.2±0.2	36.6±0.1	24.8±2.6
135±8	79.6±5.9	483±57	30.56±2.06	20.87±1.88	52.2±4.3	1.98±0.18	3.28±0.45	37.8±0.2	37.2±0.2	136.3±15.8
113±6	76.3±3.4	1012±125	11.62±1.67	12.59±1.07	22.3±4.9	1.40±0.25	2.96±0.48	38.2±0.1	37.5±0.2	30.4±4.8

Temperature Effects

Several significant changes occurred as a result of heat stress and were found irrespective of the presence of ozone. Ventilation ($\dot{V}_E$ BTPS) was higher in condition B4 (the most severe heat stress as judged by WBGT index) than in all other conditions. This was accompanied by a higher oxygen consumption in B4 than in B1 or B3, the less severe thermal stress conditions. Despite the compensating increase in $\dot{V}_{O_2}$ in the hot environment, the oxygen consumed per heart beat (oxygen pulse) was higher in the coolest environment, B1. As expected, the rectal temperature (T_{re}), mean body temperature ($\overline{T}_b$), and mean skin temperature ($\overline{T}_{sk}$)were higher in the hotter environment. The T_{re} was significantly higher in B4 than in B1. However, $\overline{T}_{sk}$ showed a progressive rise with increasing heat stress, B4 > B3 > B2 > B1. Mean body temperature showed a similar progressive rise except that B2 and B3 were not significantly different, B4 > B3, B2 > B1. The increased heat stress is reflected in a higher tissue conductance. The combination of increased body temperature and increased ventilation resulted in a significantly higher respiratory heat loss in condition B4. When correlated with web bulb globe temperature index (WBGT), rectal temperature showed a significant linear correlation ($P < 0.01$) ($r = 1.00$). Oxygen pulse ($r = -0.96$) and mean body temperature ($r = 0.97$) were also significantly correlated with WBGT. These findings are supported by an analysis of variance which indicated a rise of rectal, mean skin, and mean body temperature with increasing thermal stress, as anticipated.

Clinical Observations

Effects of the environment on the normal human are manifested frequently as signs and symptoms referable to the particular physiological system affected. When young adult males are exposed for two hours to an environment containing 0.5 ppm of O_3 and made to work at varying levels of ambient heat and humidity, they develop symptoms and signs mainly in the mid-respiratory tract. These consist of substernal discomfort, dryness of the throat, difficulty in deep inspiration, tenderness of the trachea, occasionally chest

pain, cough and auscultatory rales. General symptoms also may occur and consist of slight nausea, dizziness, headache, and syncope.

Fifty-eight observations on eight subjects exposed to all ambient temperatures and ozone led to a meaningful deduction that exposure as described produces one or more of the above clinical symptoms. A chi-square analysis gave $\chi = 25.5$; $P < 0.01$. The following summarization presents this data:

	Filtered Air	0.5 ppm O_3
No symptoms	25	7
Symptoms	3	23

When we look at the data relating the various ambient conditions to symptoms singly or in combination, it is apparent that at condition 8 [ambient temperature (T_a) = 40°C, relative humidity (rh) = 80%, 0.5 ppm O_3] symptoms occurred 20 times in eight runs, whereas at code 4 (T_a = 40°C, rh = 80%, FA) symptoms appeared twice and neither time were they referable to the respiratory tract (Fig. 3). Also to be noted is the high number of subjects (7) with general symptoms on exposure to ozone with high heat and humidity. Thus it would appear that a hot, humid environment containing 0.5 ppm O_3 produces distinct signs and symptoms of respiratory tract dysfunction, in combination with evidence of general stress response. The presence of O_3 seems to contribute to the latter by its specific effects on the respiratory tract.

The nature of the respiratory symptoms suggests that the ozone affects mainly the components of the mid-respiratory tract (laryngotracheal and bronchial). Somewhat surprising is the absence of symptoms in the conjunctivae, the nasal passages, and the oropharynx. This contrasts with effects produced by peroxyacetylnitrate (PAN), where eye symptoms and nasal congestion are seen early in exposure. When general symptoms occurred (nausea, syncope, weakness, dizziness),

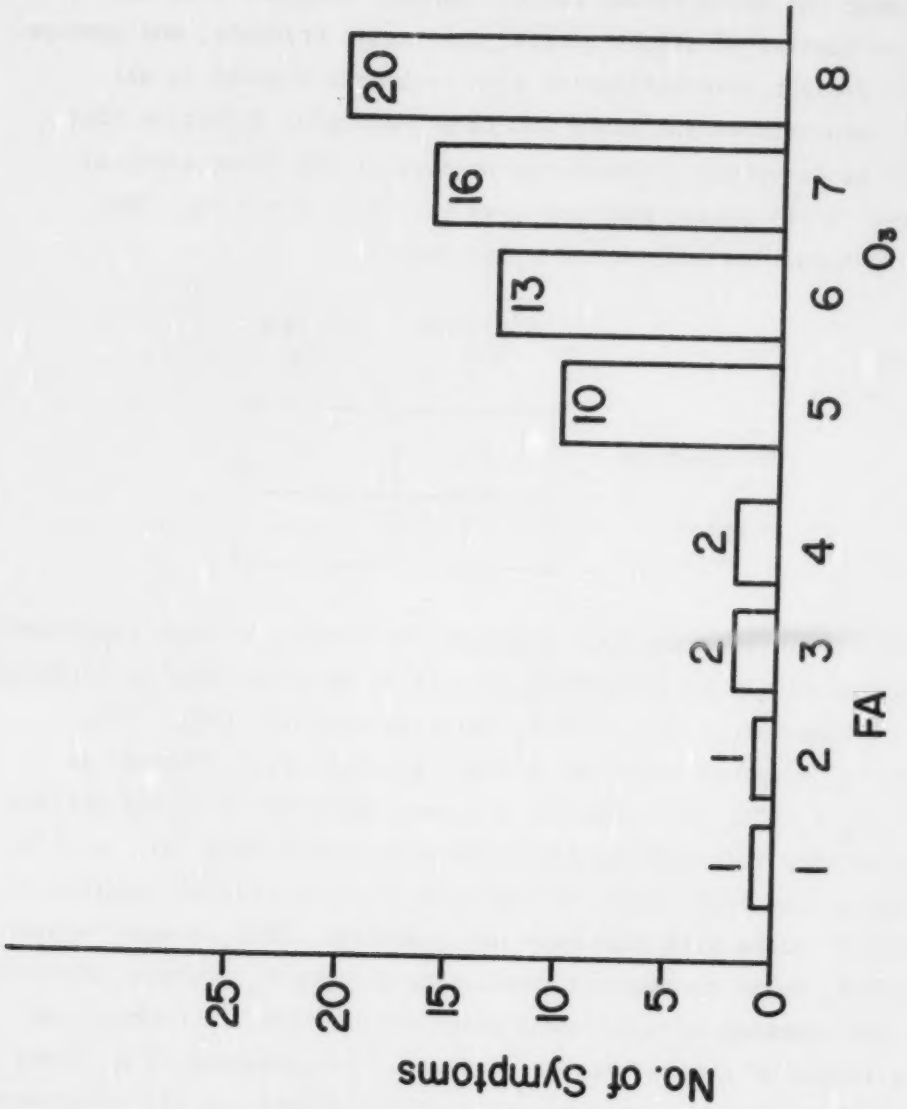

FIGURE 3.

Frequency of clinical symptoms observed consequent to exposure to the eight conditions (four filtered air and four 0.5 ppm ozone).

they subsided on terminating exposure in the chamber, or very soon afterward. Headache persisted up to 12 hours in two subjects. Two other subjects noted persistence of substernal tightness.

The following protocol abstracts provide examples of runs under the most stressful conditions:

EXPERIMENT NO. 7707

Code 8 (T_a = 40°C, rh = 80%, 0.5 ppm O_3)

Time: 1230 -- Pre-exposure blood drawn. No symptoms. Chest clear. T_{re} = 37.4°C, HR = 72.

1315 -- Into chamber. HR = 90.

1400 -- T_{re} = 37.6°C, HR = 113. Sweating on torso.

1432 -- Start walk. T_{re} = 37.6°C, HR = 93.

1450 -- T_{re} = 37.8°C, HR = 150.

1500 -- Face flushed. Sweating = 2 plus. T_{re} = 38.0°C, HR = 170.

1502 -- End walk. Feels ok but "hot."

1510 -- Occasional cough. Breathing "hot" (in chamber). T_{re} = 38.4°C, HR = 120.

1520 -- Sweating = 3 plus. Flushed. T_{re} = 38.5°C, HR = 120.

1530 -- Deep breath hurts. Out of chamber. Feels tired and hot. No other respiratory symptoms. Exam normal except for flushed face.

1540 -- Post-exposure blood drawn. Follow-up normal.

EXPERIMENT NO. 7700

Code 7 (T_a = 35°C, rh = 40%, 0.5 ppm O_3)

Time: 1315 -- No symptoms. No cold. Chest clear. Pre-exposure blood drawn.

1342 -- Into chamber. T_{re} = 37.0°C. Ozone exposure at 1352.

1440 -- T_{re} = 37.2°C, HR = 87.

1455 -- Start walk. HR = 90, T_{re} = 37.4°C.

1500 -- HR = 118, T_{re} = 37.8°C.

1525 -- End walk. HR = 150, T_{re} = 38.0°C. Coughing moderately. Tight chest.

Time: 1530 -- Frequent cough during pulmonary function tests.
1532 -- Slight nausea. Slight pallor. Coughing. BP = 108/65, HR = 140.
1535 -- Frequent yawning.
1540 -- Final period. Slight recovery from symptoms. Less coughing. Feels better but still pale.
1555 -- Out of chamber. Much improved. Chest clear. No rales after cough but breath sounds exaggerated.
1600 -- Post-exposure blood drawn.

FOLLOW-UP NOTE: 2/26/75 -- Felt chest tightness till 6 p.m. that night. Slept ok. No cough.

Four of these subjects had spent their childhood and youth in a smoggy area of California (Pomona, Pasadena, or Century City); the others in various parts of the United States. All the subjects were nonsmokers.

Subjective Analysis of Ozone Exposures

All subjects answered a questionnaire at the end of each exposure. The questionnaire contained 33 questions concerning the subject's physical and psychological feelings following the experiment. The questionnaire was divided into three distinctive areas. The first dealt with physical factors (dryness of the throat or irritation of the eyes, etc.), the second was concerned with central nervous system changes (fatigue, lack of energy, etc.), while the third related to psychological states (pleasure, happiness, anxiety, or depression.

The data obtained from this questionnaire was analyzed by a two-factor analysis of variance (pollutants x ambient air condition). The results demonstrated several significant changes in subjective responses as a function of ozone, but not as a function of ambient temperature; nor were there any interactions between the two. The significant changes found as a function of ozone were for the most

part in the physical portion of the scale which showed an overall difference at the 0.05 level of significance. More specifically, subjects felt significantly more chest tightness, throat irritation, headaches, heart pounding and, overall, less comfortable. There was a lack of complaints of eye irritation as a function of the ozone exposures.

Subjects felt significantly less vigorous, less refreshed, less energetic and reported greater dizziness as a function of the ozone treatments as compared to filtered air ($P < 0.05$). There were no significant changes in psychological state accompanying ozone exposure. This was evident on questions concerning pleasure, happiness, anxiety, and depression, which failed to differentiate any of the treatment conditions.

Overall it appeared that the subjects' feeling about his physical state correlated rather well with the pulmonary changes as a function of ozone exposure. On the other hand, the subjects' complaints of fatigue and lack of energy appear to be of a CNS origin, as the metabolic data do not corroborate a higher level of work performed under exposure to ozone.

DISCUSSION

Pulmonary Function

Overall, ozone had a marked effect on the lung, causing a reduction in vital capacity, primarily a result of a decreased inspiratory capacity, as well as a decline in maximum expiratory flow throughout the full range of vital capacity.

A decline in vital capacity could occur as a result of a decreased maximum inspiration or a rise in residual volume. A decrease of inspiratory capacity does not rule out the latter, as this could be a result of an increase in mean chest position as suggested by Silverman et al. (unpublished). However, the lack of a significant increase in residual volume would seem to confirm that the decrease in inspiratory capacity was the result of a decreased maximal inspiration despite a

small (100 ml) but significant increase in functional residual capacity. A decline in TLC is consistent with the findings of Clamann and Bancroft (60) as well as some of the subjects studied by Silverman et al. (61). However, Hazucha et al. (43) found the decline in vital capacity in their subjects was due to an increase of residual volume with no significant change in the total lung capacity. It is not clear whether this change is dependent on the type of ozone exposure; more specifically could it depend on the amount and type of exercise performed, the temperature and humidity conditions during exposure, or the concentration of ozone present in the chamber atmosphere? The evidence from this study and others (27, 60, 61) would support the view that a decrease of vital capacity can occur as a result of a limitation of maximum inspiration. The difficulty noted in taking a deep breath would suggest that the decreased maximum inspiration may result from voluntary limitation of inspiratory effort due to discomfort caused by ozone stimulating the tracheo-bronchial irritant receptors. Whether or not this limitation may be overridden in exceptionally well motivated subjects is open to question. We made every effort to ensure that our subjects performed the vital capacity maneuvers to the best of their ability, however it could not be determined whether their effort was voluntarily or physiologically limited.

The influence of the environmental conditions during exposure on the ozone-induced decrease in vital capacity is partially clarified in this study. When ozone exposure was combined with heat stress, the greatest decline in VC occurred, suggesting that ambient temperature and humidity are important in the degree of effect experienced during ozone exposure. Whether the thermal effect is synergistic with ozone or whether the effects of temperature and humidity are merely additive is not clear. A decline in VC was also observed in condition B4 when no ozone was present, which indicates that increased heat and humidity alone can result in a decrease in vital capacity. The cause of this change is unclear. There is some possibility of a rise in central blood volume as a result of heat stress but if such a blood volume increase occurred, an increase in residual volume would be expected, and this was not found. The lack of a decline in inspiratory

capacity or in total lung capacity makes this decline in vital capacity more difficult to explain — possibly a nonsignificant change in both measures contributed to a significant change in VC.

The maximum expiratory flow is similar to that found in other studies (27, 42, 61). It may be significant, however, that the largest change occurred after the exercise period. A decline in $FEV_{1.0}$, MMEF, or MEF50% is generally attributed to an increase in large airways resistance. This is most likely a result of a reflex bronchoconstriction secondary to stimulation of tracheo-bronchial irritant receptors. An increase in R_{aw} measured at FRC would support this view. The decline in $FEV_{1.0}$ (5.8%) and in MEF50% (14.6%) is of the same order of magnitude that would be expected when an effective dose is calculated using the formula of Silverman et al. (61) (i.e. in this study effective dose = 1.5 rest dose). That the subjects did not voluntarily limit their expiratory effort is confirmed by the lack of change in FEV/VC ratio. However, a decline in MVV regardless of exposure conditions may suggest a lack of motivation following 2 hours of test procedures despite the encouragement given for this effort.

It is interesting that the greatest change in pulmonary function occurred immediately after the exercise period (Table 6). The results of other studies would suggest a slight improvement in some pulmonary function measures (notably $FEV_{1.0}$) immediately following exercise (62). In the control condition (code 1), there was either no change (VC) or a slight increase ($FEV_{1.0,2.0,3.0}$) in the measured function. With ozone exposure, there was a more marked decrease in vital capacity and $FEV_{1.0}$ immediately after exposure. In the subsequent measurement period (~25 min post exercise) many of the changes had begun to show improvement despite continued exposure to ozone. There is some similarity between the observed decline in FVC and $FEV_{1.0}$ following exercise and that observed in exercise-induced asthma (63). With this affliction, the greatest decline in FVC and $FEV_{1.0}$ occurs within 5-10 min following exercise and then begins to return towards "normal."

The significant decrease in work $\dot{V}_{O_2}$ during all ozone exposures could be a real occurrence or an error due to calculation of $\dot{V}_{O_2}$ by

the Haldane transform, which would not account for an increased inspired O_2 due to possible excess O_2 entering the room consequent to generation of O_3 from 100% O_2. If the latter were true, then inspired O_2 would have to be 21.34-21.44% rather than the ambient value of 20.93%. Such differences in inspired oxygen concentration could not be demonstrated by analysis of the oxygen content of the room by either Haldane or gas chromatographic analysis. The highest value so obtained was 20.99% O_2 — insufficient to explain the differences observed. If such O_2 changes had occurred, $\dot{V}O_2$ at rest and post-exercise should have shown a decline in O_3 atmosphere. Although occasionally the O_3 values were lower, they were also the same or higher. No statistical differences were noted at these rest periods in contrast to the significant difference ($P < 0.05$) during exercise.

The lack of a significant change in any cardiovascular parameters as a result of ozone exposure is not surprising in light of the instability of ozone and the probability that it does not reach the circulation as molecular O_3. Despite suggestive changes in red cell enzymes (64) which demonstrate some extrapulmonary effect of ozone, there is no significant effect on the cardiac output or heart rate either at rest or during exercise. It should be noted that the cardiac output and heart rate are fairly crude indices of function or control in the cardiovascular system and we are unable to rule out more subtle changes in the cardiovascular system which may occur over longer periods of exposure to ozone.

SECTION VIII

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SECTION IX

GLOSSARY OF TERMS, ABBREVIATIONS, AND SYMBOLS

(1) RESPIRATORY MEASUREMENTS

Parameter and Formula	Abbreviation	Units
1. Ventilatory Volume		
(a) $\dot{V}_E$ (uncorrected volume)	$\dot{V}_E$	liters/min
(b) $\dot{V}_E \text{ BTPS} = \dot{V}_E \times \frac{310}{273 + \text{gas temp.}} \times \frac{BP - WVP}{BP - 47}$	$\dot{V}_E$ BTPS	liters/min
(c) $\dot{V}_E \text{ STPD} = \dot{V}_E \times \frac{P_{bar} - P_w}{760} \times \frac{273}{273 + \text{gas temp.}}$	$\dot{V}_E$ STPD	liters/min
	P_{bar} = barometric pressure	
	P_w = water vapor pressure at the gas temp.	
2. Respiratory Rate	RR or f_R	breaths/min
3. Tidal Volume		
$\frac{\dot{V}_E}{RR}$	V_T	ml/breath
4. Ventilatory Equivalence Ratio		
$\frac{\dot{V}_E \text{ BTPS}}{\text{Oxygen Uptake}}$	$\dot{V}_E \text{ BTPS}/\dot{V}_{O_2}$	$\frac{\text{liters breathed}}{\text{liters } O_2}$

(2) METABOLIC MEASUREMENTS

Parameter and Formula	Abbreviation	Units
1. Oxygen Uptake		
(a) $\frac{\dot{V}_E \text{ STPD} \times \text{True } O_2\%}{100}$	$\dot{V}O_2$	liters O_2/min
(b) $\frac{\dot{V}_E \text{ STPD} \times \text{True } O_2\% \times 1000}{100 \times \text{Pre Wt}}$	$\dot{V}O_2$	ml O_2/kg·min^{-1}
(c) $\frac{\dot{V}_E \text{ STPD} \times \text{True } O_2\% \times 1000}{100 \times \text{Lean Body Mass}}$	$\dot{V}O_2$	ml O_2/LBM·min^{-1}
2. True Oxygen		
$(\%N_2 \times 0.265) - \%O_2$ in expired air	True O_2	%
3. Respiratory Exchange Ratio	R	no units
$\frac{\% \text{ Expired } CO_2}{\% \text{ Expired } O_2}$ or $\frac{CO_2 \text{ Production}}{\text{Oxygen Uptake}}$	$\frac{\dot{V}_E\ CO_2}{\dot{V}O_2}$	
4. Excess Carbon Dioxide	Excess CO_2	liters
$\dot{V}_E \text{ STPD} \times \frac{(\%CO_2 \text{ Expired} - 0.03)}{100} - \dot{V}O_2 \times 0.75$		
5. Maximal Aerobic Power	$\dot{V}O_{2\ max}$	liters/min
and/or		ml O_2/kg·min^{-1}
Maximal Aerobic Capacity		ml O_2/LBM·min^{-1}

(The largest value of oxygen uptake obtained when a subject performs maximal exhaustive work.)

Parameter and Formula	Abbreviation	Units
6. Percent of Maximal Oxygen Uptake	$\%\dot{V}O_{2\ max}$	%

$$\frac{\dot{V}O_2}{\dot{V}O_{2\ max}} \times 100$$

7. Energy Production

cal/liter O_2 = 1.27604 × R + 3.82041

(a) = cal/liter O_2 × 60 × liter O_2/min	M	kcal/h
(b) = $\frac{a}{\text{Pre Wt, in kg}}$	M	$kcal/kg \cdot h^{-1}$
(c) = $\frac{a}{BSA}$	M	$kcal/m^2 \cdot h^{-1}$
(d) = c × 1.163	M	$watts/m^2$

(3) CARDIOVASCULAR

1. Cardiac Output = Stroke Volume × HR	$\dot{Q}$	liters/min

$$\frac{\dot{V}O_2}{C_aO_2 - C_vO_2}$$

2. Cardiac Index	CI	$liters/min \cdot m^{-2}$

$$\frac{\dot{Q}}{\text{Body Surface Area, in } m^2}$$

Body Surface Area = BSA

Parameter and Formula	Abbreviation	Units
3. Cardiac Work	CW	kg·m/min
$\frac{SP \times 13.6 \times \dot{Q}}{1000}$		
4. Heart Rate	HR, f_C	beats/min
5. Stroke Volume	SV	ml/beat
$\frac{\dot{Q}}{HR}$		
6. Stroke Index	SI	ml/beat·m^{-2}
$\frac{SV}{BSA}$		
7. Stroke Work	SW	g·m/beat
$\frac{SP \times 13.6 \times SV}{1000}$		
8. Oxygen Pulse	O_2 Pulse	ml O_2/beat
$\frac{\dot{V}_{O_2} \times 1000}{HR}$		

Parameter and Formula	Abbreviation	Units
9. Arteriovenous Oxygen Difference	$(a - v)O_2$ diff.	ml O_2/liter blood
$\frac{\dot{V}_{O_2} \times 1000}{\dot{Q}}$		
10. Systolic Pressure (Arterial)	SP, P_{sys}	torr
11. Diastolic Pressure (Arterial)	DP, P_{dias}	torr
12. Mean Blood Pressure (Arterial)	MBP, $\overline{P}_{bl}$	torr
$\frac{SP - DP}{3} + DP$		
13. Pulse Pressure	PP	torr
SP - DP		
14. Total Peripheral Resistance	TPR	dyn·sec cm^{-5}
$\frac{1.333 \times 60 \times MBP}{\dot{Q}}$		

(4) PULMONARY

1. Forced Vital Capacity	FVC	(ml, ml/kg) ml/m^2

Parameter and Formula	Abbreviation	Units
2. Timed Forced Expired Volumes (1.0, 2.0, and 3.0 seconds)	$FEV_{1.0}$ $FEV_{2.0}$ $FEV_{3.0}$	ml
3. Forced Expired Volumes as a percentage of Forced Vital Capacity $\frac{FEV_{1.0}}{FVC} \times 100$	$FEV_{1.0}/\%FVC$ $FEV_{2.0}/\%FVC$ $FEV_{3.0}/\%FVC$	%
4. Inspired Capacity	IC	ml
5. Expiratory Reserve Volume	ERV	ml
6. Functional Residual Capacity	FRC	ml
7. Residual Volume	RV	ml, ml/kg, ml/m^2
8. Total Lung Capacity VC + RV	TLC	ml, ml/kg, ml/m^2
9. Residual Volume/Percent Total Lung Capacity $\frac{RV}{TLC} \times 100$	RV/%TLC	%
10. Maximal Mid-Expiratory Flow	MMEF	liters/sec

Parameter and Formula	Abbreviation	Units
11. Maximal Voluntary Ventilation	MVV	liters/min
12. Maximal Expiratory Flow @ 50% of Vital Capacity	MEF50%	liters/sec
13. Maximal Expiratory Flow @ 25% of Vital Capacity	MEF25%	liters/sec

(5) HEMATOLOGIC

1. Hemoglobin	Hb	mMoles/liter, g%
2. Hematocrit	Hct	%
3. Plasma Proteins		g%
4. Lactate	Hla	mEq/liter
5. Carboxyhemoglobin	HbCO	%, vol%

$$\frac{\text{HbCO (vol\%)}}{\text{Hb (g\%)} \times 1.39} \times 100$$

(6) TEMPERATURE REGULATORY

1. Rectal Temperature	T_{re}	°C
2. Forehead Temperature	T_{hd}	°C
3. Arm Temperature	T_{arm}	°C
4. Finger Temperature	T_{fing}	°C
5. Thigh Temperature	T_{thi}	°C

Parameter and Formula	Abbreviation	Units
6. Calf Temperature	T_{calf}	°C
7. Chest Temperature	T_{ch}	°C
8. Toe Temperature	T_{toe}	°C
9. Room Temperature	T_{rm}	°C
10. Air Temperature	T_a	°C
11. Radiant Temperature	T_r	°C
12. Globe Black Temperature	T_g	°C
13. Wall Temperature	T_{wall}	°C
14. Wet Bulb Temperature	T_{wb}	°C
15. Mean Skin Temperature	$\overline{T}_{sk}$	°C
$\overline{T}_{sk} = 0.07\ T_{hd} + 0.36\ T_{ch} + 0.05\ T_{fing} + 0.14\ T_{arm} + 0.05\ T_{toe} + 0.13\ T_{calf} + 0.20\ T_{thi}$		
16. Mean Body Temperature	$\overline{T}_b$	°C
$0.65\ T_{re} + 0.35\ \overline{T}_{sk}$		
17. Body Heat Content	BHC	$kcal/m^2$
$\frac{Pre\ Wt \times 0.83\ \overline{T}_b}{BSA}$		
18. Wet Bulb Globe Temperature Index	WBGT	°C(°F)
$0.3\ T_g + 0.7\ T_{wb}$		

Parameter and Formula	Abbreviation	Units

19. Tissue Conductance — K — $kcal/m^2 \cdot h^{-1} \cdot {}^{\circ}C^{-1}$

$$\frac{kcal/m^2 \cdot h^{-1}}{T_{re} - \overline{T}_{sk}} = \frac{\text{Energy Prod}}{T_{re} - \overline{T}_{sk}}$$

20. Respiratory Evaporative Water Loss — Resp. H_2O Loss — g/h

$\dot{V}_E$ BTPS × factor × 60

(The factor is determined from density steam tables and is dependent on temp. of expired gases.)

21. Respiratory Evaporative Heat Loss — Resp. Heat Loss ($-E_r$) — $kcal/m^2 \cdot h^{-1}$

$$\frac{\text{Resp. } H_2O \text{ Loss} \times 0.58}{\text{BSA}}$$

22. Skin Evaporative Heat Loss — Evap. Heat Loss ($-E_{sk}$) — $kcal/m^2 \cdot h^{-1}$

$$\frac{[\text{Pre Wt} - \text{Post Wt} - \text{Resp. } H_2O \text{ Loss} - \text{Excess } CO_2 \text{ (g)}] \times 0.580}{\text{BSA}}$$

ALPHABETICAL LIST OF ABBREVIATIONS AND SYMBOLS USED

$(a - v)O_2$ diff.	arteriovenous oxygen difference
alveol. (A)	alveolar
AQS	air quality standards
BHC	body heat content
BMR	basal metabolic rate
BP	blood pressure
BSA	body surface area
BTPS	body temperature and pressure, saturated with water vapor
cal	calorie(s)
C_aO_2	arterial oxygen content
CI	cardiac index
cm	centimeter(s)
CNS	central nervous system
CO	carbon monoxide
CO_2	carbon dioxide
CV	closing volume
C_vO_2	venous oxygen content
CW	cardiac work
°C	degree(s) Celsius
°F	degree(s) Fahrenheit
diff.	difference
$D_{L_{CO}}$	diffusion capacity to carbon monoxide
DP	diastolic pressure
dyn	dyne(s)
ERV	expiratory reserve volume

evap.	evaporative
FA	filtered air
f_C	cardiac frequency (same as HR)
FEV	forced expired volume
$FEV_{1.0}$	forced expired volume (1.0 second)
$FEV_{2.0}$	forced expired volume (2.0 seconds)
$FEV_{3.0}$	forced expired volume (3.0 seconds)
f_R	respiratory frequency
FRC	functional residual capacity
FVC	forced vital capacity
g	gram(s)
h	hour(s)
H, ht	height
Hb	hemoglobin
HbCO	carboxyhemoglobin
Hct	hematocrit
HLa	lactate
H_2O	water
HR	heart rate (same as f_C)
IC	inspiratory capacity
K	tissue conductance
kg	kilogram(s)
LBM	lean body mass
m	meter(s)
M	energy production
max	maximal, maximum
MBP	mean blood pressure

MEF	maximal expiratory flow
MEF25%	maximal expiratory flow at 25% of vital capacity
MEF50%	maximal expiratory flow at 50% of vital capacity
mEq	milliequivalent(s)
min	minute(s)
ml	milliliter(s)
MMEF	maximal mid expiratory flow
mMoles	millimoles
MVV	maximum voluntary ventilation
N_2	nitrogen
NO_x	oxides of nitrogen
O_2	oxygen
O_3	ozone
P	probability of wrongfully rejecting the null hypothesis (level of significance)
P_{bar}	barometric pressure
P_w	water vapor pressure
PAN	peroxyacetylnitrate
%	percent
perf.	perfusion
PP	pulse pressure
ppm	parts per million
press.	pressure
prod.	production
$\dot{Q}$	cardiac output

R	respiratory exchange ratio
R_{aw}	airway resistance
RBC	red blood cell
resp.	respiratory
rh	relative humidity
RR	respiratory rate (same as f_R)
RV	residual volume
s, sec	second(s)
SE	standard error
SI	stroke index
SO_x	sulfur oxides
SP	systolic pressure
STPD	standard temperature and pressure, dry
SV	stroke volume
SVC	slow vital capacity
SW	stroke work
syst.	systolic
T_a	ambient air temperature
T_{arm}	arm temperature
$\overline{T}_b$	mean body temperature
T_{calf}	calf temperature
T_{ch}	chest temperature
T_{fing}	finger temperature
T_g	globe temperature
T_{hd}	forehead temperature

T_r	radiant temperature
T_{re}	rectal temperature
T_{rm}	room temperature
$\bar{T}_{sk}$	mean skin temperature
T_{thi}	thigh temperature
T_{toe}	toe temperature
T_{wall}	wall temperature
T_{wb}	wet bulb temperature
temp.	temperature
TLC	total lung capacity
TLV	threshold limit values
TPR	total peripheral resistance
V	volume
$\dot{V}$	timed ventilatory volume
$\dot{V}_A$	alveolar ventilation
$\dot{V}_A/\dot{Q}$	ventilation perfusion ratio
$\dot{V}_E$	ventilatory volume, expired
$\dot{V}O_2$	oxygen uptake
$\dot{V}O_{2\ max}$	maximal aerobic capacity (maximal aerobic power)
V_T	tidal volume
VC	vital capacity
W, wt	weight
WBGT	wet bulb globe temperature index
yr	year(s)
χ^2	statistical datum derived in the chi-square test

SECTION X

APPENDICES

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APPENDIX A

COMPLETE MEAN DATA WAS FORWARDED EARLIER.

INDIVIDUAL DATA ARE STORED IN OUR DATA BANK.

EX.NO.	STUDY	DATE	AGE	SEX	PRE WT.	POST WT.	HT.CM	BSA	B°	PRE TEMP	POST TEMP	HRS.PA	RM TEMP	REL.HUM	BP	TIME
7708	POLUTD	2-26-75	20	M	63.20	62.80	177.8	1.80	.00	37.50	37.60	1	25.0	45	764	1300

PERIOD	EVENT	V/BIA	RR	% O2	% CO2	GAS TEMP	ET CO2	V STPD	V BTPS	T O2	L/O2/MIN	ML O2/KG	O2 P	VE	% MAX	HR
1	P1 2-4	10.6	18	17.58	2.85	19.0	5.01	9.75	11.73	3.91	0.34	5.41	4.07	34.33	0.10	84
8	P4 2-4	10.7	20	17.88	2.55	19.1	4.85	9.83	11.84	3.21	0.32	4.99	3.50	37.54	0.09	90
13	P6 2-4	31.2	17	16.34	4.17	19.1	8.26	28.68	34.52	4.72	1.35	21.44	11.92	25.47	0.38	123
18	P8 2-4	8.9	22	17.69	2.71	19.1	5.37	8.18	9.85	3.40	0.28	4.41	3.87	35.36	0.08	72

MAXIMUM OXYGEN UPTAKE = 3.59

METABOLIC DATA: EX. NO. 7708

	R	EXCESS CO2	KCAL/KG-HR	KCAL/HR	KCAL/M2-HR	ML O2/LBM	WATTS/M2	TIDAL VOL. ML
1	0.80	0.0186	1.56	98.58	34.75	0.00	63.678	651.78
8	0.79	0.0114	1.43	90.51	50.24	0.00	58.477	591.86
13	0.88	0.1710	6.30	397.91	221.05	0.00	257.096	2030.34
18	0.79	0.0104	1.27	79.95	44.42	0.00	51.660	447.54

TEMPERATURES: 7708

EVENT	RECTAL	FOREHEAD	ARM	FINGER	THIGH	CALF	CHEST	ABDOMEN	_____	RADIANT	WALL	RM.A
P1 2-4	37.4	35.6	30.6	32.9	30.4	30.9	31.2	31.2	0.0	23.4	0.0	23.4
P1 14-15	37.3	35.6	31.1	32.3	30.6	30.9	31.4	31.4	0.0	23.9	0.0	24.0
P2 5-6	37.2	35.7	31.2	32.0	30.2	30.9	31.0	31.0	0.0	25.3	0.0	24.6
P2 10-11	37.2	35.7	31.1	32.6	30.2	30.9	31.3	31.0	0.0	24.8	0.0	23.9
P3 4-5	37.2	35.7	31.0	32.6	30.2	31.1	30.7	30.7	0.0	23.8	0.0	23.9
P3 9-10	37.1	35.6	31.0	32.6	30.9	30.2	31.3	31.5	0.0	23.9	0.0	24.0
P3 14-15	37.1	35.8	31.1	32.1	30.1	30.9	30.3	31.4	0.0	24.1	0.0	24.0
P4 2-4	37.1	35.9	31.1	32.1	30.1	30.6	30.7	31.2	0.0	24.2	0.0	24.0
P4 14-15	37.1	35.7	31.3	32.3	30.9	31.0	31.5	31.6	0.0	23.9	0.0	24.0
P5 4-5	37.4	35.5	31.4	32.3	31.2	31.5	32.4	31.7	0.0	24.0	0.0	24.6
P5 9-10	37.5	35.4	31.5	32.3	31.4	32.0	32.8	31.8	0.0	24.5	0.0	24.6
P5 14-15	37.6	35.3	31.6	32.3	31.8	32.4	33.4	31.9	0.0	24.6	0.0	24.7
P6 2-4	37.6	35.2	31.7	32.3	32.4	33.3	33.5	32.8	0.0	24.7	0.0	24.8
P6 14-15	37.7	35.1	31.8	32.3	32.9	33.5	33.7	32.1	0.0	24.8	0.0	24.9
P7 4-5	37.7	35.0	31.8	32.3	33.5	34.9	34.8	32.2	0.0	25.1	0.0	25.1
P7 9-10	37.6	34.7	31.7	32.3	33.3	34.7	34.7	32.3	0.0	25.0	0.0	24.9
P7 14-15	37.7	34.5	31.8	32.3	33.1	34.5	33.6	32.8	0.0	24.9	0.0	24.8
P8 2-4	37.6	34.5	31.7	32.3	33.1	34.3	34.4	33.1	0.0	24.8	0.0	24.7
P8 14-15	37.6	35.1	31.9	32.3	32.8	33.8	32.1	30.9	0.0	24.8	0.0	24.7

ROOM TEMP. MEAN 24.43 RADIANT TEMP. MEAN 24.41

EVENT	MEAN SKIN TEMP.	MEAN BODY TEMP.	BODY HEAT KCAL/M2	RADIATION KCAL/M2-HR	TISSUE CONDUCT.	RESP.EVAP. KCAL/M2-HR	SKIN EVAP. KCAL/M2-HR	EXCESS CO2 GRAMS/HR	RESP. H2O GM/HR
P1 2-4	31.4	35.3	1028.9	33.3	9.2	6.8	52.4	3.69	21.3
P1 14-15	31.5	35.3	1028.1	32.0	0.0	0.0	0.0	0.00	0.0
P2 5-6	31.3	35.1	1023.7	29.2	3.0	0.0	0.0	0.00	0.0
P2 10-11	31.3	35.1	1024.3	30.7	0.0	0.0	0.0	0.00	0.0
P3 4-5	31.2	35.1	1023.2	31.1	0.0	0.0	0.0	0.00	0.0
P3 9-10	31.6	35.2	1025.0	32.5	0.0	0.0	0.0	0.00	0.0
P3 14-15	31.2	35.0	1021.0	29.8	0.0	0.0	0.0	0.00	0.0
P4 3-4	31.2	35.0	1021.4	29.5	0.6	6.9	52.6	2.75	21.5
P4 14-15	31.8	35.2	1026.6	33.0	0.0	0.0	0.0	0.00	0.0
P5 4-5	32.0	35.5	1034.7	33.6	0.0	0.0	0.0	0.00	0.0
P5 9-10	32.2	35.6	1038.5	32.4	0.0	0.0	0.0	0.00	0.0
P5 14-15	32.4	35.8	1043.0	33.1	0.0	0.0	0.0	0.00	0.0
P6 2-4	32.7	35.9	1045.0	33.8	65.0	20.1	31.9	25.83	62.8
P6 14-15	32.9	36.0	1049.6	34.3	0.0	0.0	0.0	0.00	0.0
P7 4-5	33.2	36.1	1052.5	34.3	0.0	0.0	0.0	0.00	0.0
P7 9-10	33.3	36.1	1051.4	35.1	0.0	0.0	0.0	0.00	0.0
P7 14-15	33.1	36.1	1051.5	34.7	0.0	0.0	0.0	0.00	0.0
P8 2-4	33.2	36.1	1051.4	35.9	13.2	5.7	53.9	2.45	17.9
P8 14-15	32.4	35.8	1042.7	32.1	0.0	0.0	0.0	0.00	0.0

EX.NO.	STUDY	DATE	AGE	SEX	PRE WT.	POST WT.	HT.CM	M2A	BP	PRE TEMP	POST TEMP	HRS.PA	RM TEMP	REL.HUM	BP	TIME
7632	POLUTD	01-14-75	24	M	74.1	73.6	177.8	1.92	.00	37.4	37.6	2	25.0	45	763	1230

PERIOD	EVENT	CARDIAC OUTPUT L/MIN.	HEART RATE BEATS/MIN.	L O2/MIN.	SYSTOLIC PRESSURE	DIASTOLIC PRESSURE	STROKE VOL. ML/BEAT	STROKE INDEX ML/BEAT-M2
1	P1 4-6	5.900	87.0	0.29	113.0	80.0	67.82	35.32
2	14-15	0.000	0.0	0.00	0.0	0.0	0.00	0.00
3	P2 5-6	0.000	84.0	0.00	119.0	80.0	0.00	0.00
4	10-11	0.000	78.0	0.00	118.0	70.0	0.00	0.00
5	P3 5-6	0.000	77.0	0.00	0.0	0.0	0.00	0.00
6	10-11	0.000	80.0	0.00	117.0	83.0	0.00	0.00
7	14-15	0.000	75.0	0.00	118.0	80.0	0.00	0.00
8	P4 5-6	4.100	81.0	0.16	124.0	80.0	50.62	26.36
9	14-15	0.000	0.0	0.00	0.0	0.0	0.00	0.00
10	P5 5-6	0.000	113.0	0.00	124.0	80.0	0.00	0.00
11	10-11	0.000	117.0	0.00	133.0	84.0	0.00	0.00
12	14-15	0.000	125.0	0.00	0.0	0.0	0.00	0.00
13	P6 5-6	15.300	134.0	1.31	125.0	74.0	114.18	59.47
14	14-15	0.000	134.0	0.00	134.0	74.0	0.00	0.00
15	P7 5-6	0.000	90.0	0.00	126.0	78.0	0.00	0.00
16	10-11	0.000	91.0	0.00	0.0	0.0	0.00	0.00
17	14-15	0.000	0.0	0.00	0.0	0.0	0.00	0.00
18	P8 5-6	7.600	79.0	0.22	114.0	72.0	96.20	50.11
19	14-15	0.000	0.0	0.00	0.0	0.0	0.00	0.00

Ex.NO. 7032

PERIOD	EVENT	CARDIAC INDEX L/MIN-M2	A-V O2 DIFF. ML O2/L	TOT.PERIPH.RES. DYNES.SEC.CM-5	PULSE PRESS.	MEAN BLOOD PRESSURE	STROKE WORK GRAMS-M/BEAT	CARDIAC WORK KG-M/MIN.	SYST. INDEX
1	P1 4-6	3.07	48.56	1220.03	30.00	90.00	101.453	8.626	9570
2	14-15	0.00	0.00	0.00	0.00	0.00	0.000	0.000	0
3	P2 5-6	0.00	0.00	0.00	30.00	90.00	0.000	0.000	9240
4	10-11	0.00	0.00	0.00	48.00	66.00	0.000	0.000	9204
5	P3 5-6	0.00	0.00	0.00	0.00	0.00	0.000	0.000	0
6	10-11	0.00	0.00	0.00	34.00	94.33	0.000	0.000	9360
7	14-15	0.00	0.00	0.00	36.00	92.67	0.000	0.000	8850
8	P4 5-6	2.14	39.69	1846.69	44.00	94.67	85.361	6.914	10044
9	14-15	0.00	0.00	0.00	0.00	0.00	0.000	0.000	0
10	P5 5-6	0.00	0.00	0.00	44.00	94.67	0.000	0.000	14012
11	10-11	0.00	0.00	0.00	66.00	86.00	0.000	0.000	15210
12	14-15	0.00	0.00	0.00	0.00	0.00	0.000	0.000	0
13	P6 5-6	7.97	65.39	477.44	62.00	91.33	195.657	26.216	18684
14	14-15	0.00	0.00	0.00	60.00	94.00	0.000	0.000	17956
15	P7 5-6	0.00	0.00	0.00	48.00	94.00	0.000	0.000	11340
16	10-11	0.00	0.00	0.00	0.00	0.00	0.000	0.000	0
17	14-15	0.00	0.00	0.00	0.00	0.00	0.000	0.000	0
18	P8 5-6	3.96	28.83	905.04	42.00	86.00	149.152	11.783	9086
19	14-15	0.00	0.00	0.00	0.00	0.00	0.000	0.000	0

EX.NO.	STUDY	DATE	AGE	SEX	PRE WT.	POST WT.	HT.CM	BSA	B*	PRE TEMP	POST TEMP	HRS.PA	RM TEMP	REL.HUM	BP	TIME
7747	POLUTO	03-20-75	28	M	78.90	78.70	184.9	2.03	.30	37.70	37.70	1	2.5	45	760	1000

EVENT	PERIOD	FUREARM BLOODFLOW ML/100ML.MIN	% CHANGE	HAND BLOODFLOW ML/100ML.MIN	% CHANGE	TOTAL BLOODFLOW ML/100ML.MIN	% CHANGE
P1 4-6	1	1.750	0.0	0.670	0.0	2.640	0.0
P2 6-8	3	2.480	41.7	1.730	90.4	4.210	59.5
P3(A)6-8	5	1.860	6.3	1.000	12.4	2.860	8.3
P4(A)4-6	8	2.620	49.7	0.880	-1.1	3.500	32.6
P5(B)6-8	10	0.000	0.0	0.000	0.0	0.000	0.0
P6(B)6-8	13	0.000	0.0	0.000	0.0	0.000	0.0
P7 6-8	15	2.790	59.4	8.530	854.4	11.320	328.8
P8 4-6	18	2.990	70.9	2.130	218.3	5.120	93.9

APPENDIX B

PRINTOUT OF PULMONARY FUNCTION DATA

EX.NO.	STUDY	DATE	AGE	SEX	PRE WT.	POST WT.	HT.CM	BSA	B²	PRE TEMP	POST TEMP	HRS.PA	RM TEMP	REL.HUM	BP	TIME
7032	POLUTO	01-14-75	24	M	74.1	73.6	177.8	1.92	.00	37.4	37.6	2	25.0	45	763	1230

PERIOD	EVENT	TLV ML	FVC ML	1 SEC ML	1 SEC % FVC	2 SEC ML	2 SEC % FVC	3 SEC ML	3 SEC % FVC	50% L/SEC	25% L/SEC
1	PRE EXP	7697	6071	4662	76.79	5474	90.23	5758	94.84	4.10	1.79
2	P1 REST	0	5997	4265	71.12	5434	90.56	5731	95.56	4.46	1.86
4	P2 REST	0	6330	4665	73.70	5664	89.48	6031	95.28	4.53	2.10
8	P4	0	6197	4598	74.20	5631	90.87	5947	96.77	5.86	1.67
11	P5 (B)	0	0	0	0.00	0	0.00	0	0.00	0.00	0.00
13	P6	0	0	0	0.00	0	0.00	0	0.00	0.00	0.00
16	P7 (A)	0	6330	4531	71.58	5597	88.42	5931	93.70	4.00	1.80
18	P8	0	6364	4731	74.34	5697	89.52	6064	95.29	4.56	1.96
19	POST EXP	7401	6138	4667	76.03	5530	90.09	5773	94.05	4.11	1.57

PERIOD	EVENT	IC ML	ERV ML	FRC ML	RV ML	RV/TLV %	MMF L/SEC	MBC L/MIN	RR B/MIN	TV ML	TLV/HT ML/CM	VC/HT ML/CM	TLV/KG ML/KG	VC/KG ML/KG	DLCO ML/MIN/MM H
1	PRE EXP	4058	2912	3638	1626	28.1	4.06	229.0	11	1300	43.29	34.15	103.87	81.93	0.00
2	P1 REST	0	0	0	0	0.0	3.70	0.0	16	0	0.00	33.73	0.00	80.93	17.20
4	P2 REST	0	0	0	0	0.0	3.90	0.0	15	0	0.00	35.60	0.00	85.43	0.00
6	P4	0	0	0	0	0.0	3.87	0.0	15	0	0.00	34.85	0.00	83.63	31.60
11	P5 (B)	0	0	0	0	0.0	0.00	0.0	0	0	0.00	0.00	0.00	0.00	0.00
13	P6	0	0	0	0	0.0	0.00	0.0	0	0	0.00	0.00	0.00	0.00	50.20
16	P7 (A)	0	0	0	0	0.0	3.73	0.0	17	0	0.00	35.60	0.00	85.43	0.00
18	P8	0	0	0	0	0.0	3.82	0.0	16	0	0.00	35.79	0.00	85.88	34.20
19	POST EXP	3705	2433	3696	1263	17.1	3.78	208.0	9	1120	41.63	34.52	99.88	82.83	0.00

PERIOD	EVENT	SVC 1 ML	CV 1 ML	PIF L	SVC 2 ML	CV 2 ML	DELTA_V2S L/SEC	CLOS.CAP1 ML	CC %TLV	CLOS.CAP2 ML	CC %TLV
1	PRE EXP	0	0	0.20	0	0	0.00	0	0.0	0	0.0
2	P1 REST	5997	666	0.00	5864	533	0.00	2292	29.8	2159	28.0
4	P2 REST	5997	828	0.00	6130	666	0.00	2454	31.9	2292	29.8
8	P4	5864	560	0.00	5797	563	0.00	2186	28.4	2186	28.4
11	P5 (B)	0	0	0.00	0	3	0.00	0	0.0	0	0.0
13	P6	0	0	0.00	0	0	0.00	0	0.0	0	0.0
16	P7 (A)	5797	500	0.00	5997	763	0.00	2186	27.0	2486	30.3
20	P8	5997	617	0.00	6130	766	0.00	2340	29.1	2340	29.1
24	POST EXP	0	0	0.00	0	0	0.00	0	0.0	0	0.0

PERIOD	EVENT	SIT ERV ML	SIT FRC ML	SIT RV ML	BOX FRC ML	BOX RV ML	AIR.RES. CM H2O S/.	PUL.COMP.	NAR	VENT.PERF.	DIFF.PERF.	V ALV L/MIN
1	PRE EXP	2967	3914	947	4943	1475	2.15	0.000	0.00	0.00	0.00	0.00
2	P1 REST	0	0	0	0	0	0.00	0.000	0.00	1.14	2.92	6.75
4	P2 REST	0	0	0	0	0	0.00	0.000	0.00	0.00	0.00	0.00
8	P4	0	0	0	0	0	0.00	0.000	0.00	0.78	7.71	3.10
11	P5 (B)	0	0	0	0	0	0.00	0.000	0.00	0.00	0.00	0.00
13	P6	0	0	0	0	0	0.00	0.000	0.00	1.71	3.28	26.21
16	P7 (A)	0	0	0	0	0	0.00	0.000	0.00	0.00	0.00	0.00
18	P8	0	0	0	0	0	0.00	0.000	0.00	0.62	4.50	4.73
19	POST EXP	2463	3751	1288	4540	2077	2.25	0.000	0.00	0.00	0.00	0.00

APPENDIX C

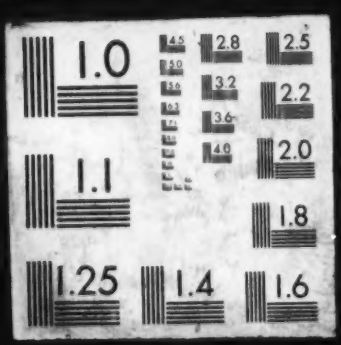
CLOSING VOLUMES AND CLOSING CAPACITIES

In the present series closing volumes were determined at frequent intervals with a minimum of two and up to four measurements at each time. Although most of our subjects had closing volumes during the preliminary testing, a few did not. It was anticipated that these latter would demonstrate a closing volume change consequent to ozone exposure. However, it became obvious that in these young subjects closing volumes were only randomly obtained and furthermore these tended to disappear more frequently following exercise. The following tabulation presents a frequency distribution of closing volumes obtained across codes and periods.

PERIOD	CODE								Σ
	1	2	3	4	5	6	7	8	
1	3	5	3	4	4	4	4	4	31
2	4	4	2	3	5	4	4	4	30
4	4	5	5	3	6	4	3	3	33
7	3	4	3	2	2	3	3	1	21
8	3	4	5	2	3	3	3	2	25
Σ	17	22	18	14	20	18	17	14	140

A Friedman (67) two-way analysis of variance (not quite the appropriate method of analysis but the best available for this purpose) indicated that there should be no reason to anticipate differences in codes or differences in periods. Disappearance of CV following exercise (periods 7 and 8) was significant at the 0.05 level, suggesting the need for further investigation of this alteration. Only two of our subjects had closing volumes present

2 OF 2
PB
252 309



during all of their tests in the eight conditions. Data (closing volume in milliliters measured from residual volume) from one of these subjects follows. No significant changes related to any of the conditions was noted.

PERIOD	CODE								$\bar{X}$
	1	2	3	4	5	6	7	8	
1	600	520	552	772	697	911	716	567	666.9
2	747	748	582	960	523	607	690	634	686.4
4	560	536	889	754	726	886	562	667	697.5
7	640	422	522	822	697	728	600	400	603.9
8	692	455	552	822	639	683	780	600	652.9
$\bar{X}$	647.8	536.2	619.4	826	656.4	763	669.6	573.6	661.5

Data from another subject, who had apparently normal closing volumes during the periods preceding exercise and disappearance after exercise, are given below.

PERIOD	CODE							
	1	2	3	4	5	6	7	8
1	---	534	442	675	---	591	---	398
2	---	534	883	427	410	830	771	451
4	---	430	204	673	547	576	136	531
7	---	771	136	---	---	589	640	---
8	---	504	340	---	---	814	484	---

The validity of closing volumes as a measure of small airway closure is questioned for these young normal subjects (55, 56). Other measures may have to be employed to obtain this information.